



## ECTU Central Office WPD ECTU\_WPD\_W6: Preparing, maintaining and reviewing the Trial Master File and Investigator Site Files

Version No:	1.0
Issue Date:	05 Feb 2024
Effective Date:	19 Feb 2024

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Document Revision History		
Version No.	Effective Date	Summary of Revisions
1.0	19 Feb 2024	Initial Creation

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## 1. INTRODUCTION

This WPD describes the procedure to be followed for preparing, maintaining and reviewing the Trial Master File (TMF) and Investigator Site Files (ISFs). This procedure applies to the trial management team in ECTU when set up and maintenance of the TMF has been delegated to ECTU from ACCORD and/or the provision of ISFs to sites is an ECTU responsibility. For studies not sponsored by ACCORD the TM must check the sponsorship agreement to confirm which responsibilities are delegated to ECTU.

The procedure should be followed by all individuals in the trial management team. The Trial Manager (TM) is responsible for maintaining oversight of any tasks delegated to ATM/TMSOs.

## 2. INSTRUCTIONS and GUIDANCE

### 2.1 Background

The TMF folder structure follows sponsor guidelines. The paper TMF is held securely in ECTU in the locked rolling storage. At the start of the study an electronic study folder is set up on the shared drive by the TM or the study set up team ([CURRENT PROJECTS](#)) using the sponsor TMF & ISF folder structure.

The ISF is an integral part of the TMF. ISF and site-specific study documentation are stored electronically on the shared drive in the appropriate section of the TMF with the other TMF documents. A paper or, if agreed with the site, an electronic version of the ISF is provided to each site before the site opens to recruitment. Refer to ECTU\_SOP\_TM\_20 Provision of ISFs to Study Sites v2.0 for details.

Certain documents in the ISF are customised for each site (e.g., consent forms, letters, patient information sheets) and these are filed in the relevant section of the TMF. Electronic versions of the documents held in the ISF are stored in the study-specific folder on the ECTU shared drive ([CURRENT PROJECTS](#)).

It is the responsibility of each member of the Trial Management team to ensure that:

- A TMF is set-up at the start of the study and regularly maintained in order to be 'inspection ready';
- All sites are provided with an ISF prior to opening to recruitment and ECTU will provide sites with further documents for filing as and when they are available;
- TMFs are regularly reviewed and this review is documented (refer to section 2.5 for details).

### 2.2 Procedure – TMF Set up

For ACCORD sponsored studies the TMF should include the documents listed in the ACCORD document checklist CTIMP (CR001-T01) or ACCORD document checklist non-CTIMP (CR001-T02) or ACCORD document checklist Medical Device (CR001-T03).

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2.2.1 The ECTU TMF & ISF Index TM-T2 has been populated with the ACCORD document checklists. The ECTU index is an excel version of the combined TMF and ISF checklists but gives more functionality than the word versions on the ACCORD website. During study set up the ECTU TMF & ISF Index TM-T2 must be made specific for your study. Customisation can include what is to be filed electronically only and what documents will be included in the ISF. For risk assessed studies a discussion with the monitor regarding TMF & ISF index customisation should be planned after sponsor risk assessment and before the monitoring plan is completed. The study monitor must approve all customisation for risk assessed studies.

2.2.2 Study documentation is stored electronically on the ECTU drive ([CURRENT PROJECTS](#)) using the same folder structure as the TMF & ISF Index.

2.2.3 All TMF documents filed in sections 0-10 are added to the TMF & ISF Index TM-T2 excel sheet to form a comprehensive index and document version tracker. The index should be filed in section 0.1 of the TMF. It will be used to track what documents are filed in the paper TMF and what documents are filed electronically on the shared drive.

2.2.4 Additional folders for the purposes of trial management (for example, admin or finance) may be added to the study folder on the shared drive by the TM. Documents that are filed but do not form part of the TMF (for example, work instructions, trackers, draft docs) are maintained electronically only for the convenience of the study team and should not be added to the TMF & ISF Index TM-T2 nor printed for the paper TMF.

2.2.5 The TM, or delegate, will set up a paper TMF. Lever arch folders, section dividers and index labels should be re-used from existing stock where possible. Additional folders added throughout the study must contain a spine label. If additional supplies are required the TM will confirm which account codes to charge stationery.

2.2.6 Poly-pockets should not be routinely used when establishing new TMFs or maintaining existing ones as the Sponsor requires these to be removed prior to archiving which creates an administrative burden. They should only be used sparingly where it is practical to group important document sets together or there is a paper log that is in regular use and needs protection from wear and tear.

2.2.7 Every document required to be in the TMF is to be saved in the correct folder on the shared drive, ideally as a PDF. Refer to the TMF checklist in the study specific folder when you are uncertain where to file documents or if they are even required in the paper TMF. The TMSO/ATM should confirm with the TM if still unsure whether a document must be filed or where to file a document.

### **2.3 Procedure – ISF Set up**

The ISF folder structure follows the sponsor guidelines. For ACCORD sponsored studies the ISF should include the documents listed in the ACCORD document checklist CTIMP (CR001-T01) or ACCORD document checklist non-CTIMP (CR001-T02) or ACCORD document checklist Medical Device (CR001-T03). Please also refer to ECTU\_SOP\_TM\_20 Provision of ISFs to Study Sites v2.0.

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2.3.1 Use the appropriate checklist to populate the ECTU TMF & ISF Index TM-T2 that has already been set up for the TMF. Add a column for each site.

2.3.2 Once the ISF Index has been finalised the paper ISF can be set-up. Lever arch folders, section dividers and index labels can be ordered as required. The TM will confirm which account codes to charge stationery.

2.3.3 ISF folders are stored in the rolling shelves in ECTU until they are sent to sites. Due to limited space ISF folders are only to be prepared for a site once a SIV date has been confirmed by the study team. The folder(s) will either be posted/couriered to the site or taken by the TM if the initiation visit is face to face. On occasion ISFs may be prepared by a third-party vendor, as confirmed by the study team, and shipped to ECTU for checking prior to being shipped to site.

2.3.4 There may be other supplies that should be shipped to the sites with the ISF e.g., pre-paid reply envelopes, address labels, expense claim forms, stamps or study merchandise. Refer to ECTU\_SOP\_TM\_20 Provision of ISFs to Study Sites v2.0 for making up site folders.

2.3.5 Some ACCORD templates (e.g., screening log, training log, delegation log) must be made site specific before filing in the ISF.

2.3.6 Some study specific documents (e.g., GP letter, PIS, questionnaires) need to be customised and made site specific before filing in the ISF. The trial management team will liaise with the site to ensure documents are appropriately customised.

2.3.7 Every document required to be in the ISF is to be saved in the correct folder on the shared drive. The ATM /TMSO should confirm with the TM if unsure whether a document must be filed or where to file a document.

2.3.8 The ISF checklist will be used to track what is filed electronically on the shared drive, what has been filed in the paper ISF and what documents have been sent to the site for filing in the ISF.

2.3.9 All documents filed in ISFs must be added to the ECTU TMF & ISF Index TM-T2 to form a comprehensive index and document version tracker for each site.

## **2.4 Procedure – TMF / ISF Maintenance**

2.4.1 To update the ECTU TMF & ISF Index TM-T2 work through each row in the index and indicate where each document is filed. When required, new sections and dividers should be added to the paper TMF and rows can be added to the TMF/ISF index to accommodate any new documents added, and printed when required.

2.4.2 The TMF & ISF Index and other documents that are frequently updated (e.g. file note log, master contact list) can be held electronically and printed when required. The location of such electronic documents must be file noted within the paper file.

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2.4.2 Tick appropriate column/s to indicate the location(s) of each document and complete version/date when a document is filed in the TMF or has been sent to a site. Colour (other than grey) can be used to highlight which documents are missing/pending (for example, to signify that a document has been filed electronically but the paper TMF is not yet updated, or to remind the team that certain essential docs are not yet available but will be at some point or that a document is still to be sent to a site).

2.4.3 For documents that are filed in multiple ISFs but customised/signed differently between sites (for example, protocol signature page, final SIV report, site agreement) the version/date field will be modified to include 'various' and the site-specific date entered in the site column, rather than a tick. This avoids the need for a separate row for each site where the signature date differs.

2.4.4 Grey out boxes when a document should not be filed in that location. Refer to the appropriate ACCORD document checklist for guidance. Please note that if the electronic only column is greyed on the ACCORD document checklist, then a paper copy of the document must be held in either the TMF and/or the ISF. The location of any documents held electronically should be detailed on the TMF & ISF Index.

2.4.5 At the start of the study, it will have been agreed with the study monitor if site related documents held in the ISF also need to be held as a duplicate paper copy in the TMF. If the monitor has approved, then some documents (for example, delegation logs, SAE forms) can be held electronically only, and recorded as such in the ECTU TMF & ISF Index TM-T2.

2.4.6 A 'flag' should be set up in the shared mailbox to indicate key correspondence which needs to be filed and printed. These emails should remain in the inbox until they have been actioned.

2.4.7 When a new document is saved on the drive, the ECTU TMF & ISF Index TM-T2 is to be updated with document details and location. New documents should be printed for the paper TMF as soon as practical and once filed the TMF index is to be updated. The location of any electronic only documents should be added to the TMF & ISF Index.

2.4.8 New documents that need to be filed in the ISF at site/s should be customised for the site (if applicable). The documents should then be emailed or posted to all the site teams and they should be instructed to file them in their ISF. If applicable, the site teams may have to confirm receipt or may be required to undergo training before using the new document(s). In some circumstances documents may be customised by the site if requested by the trial management team and the study team should follow up with the site to obtain a copy of the site-customised document for the TMF. Site-specific customised documents are to be filed electronically in the appropriate section of the shared drive and recorded in the ECTU TMF & ISF Index TM-T2. If required, hard copies will be printed and filed in the paper TMF as appropriate.

2.4.9 During document preparation draft versions will be filed electronically on the shared drive in a 'drafts' folder in the relevant section of the TMF. Only the finalised document should be added to TMF & ISF index and filed. Documents forming part of the TMF should be saved as a PDF when possible. Word documents can be retained in case new versions need to be created.

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2.4.10 Printed documents for filing can be coded at the top right by the TM. An abbreviated document name may also be added to assist with filing if necessary. When filing the TMSO/ATM should confirm the document is saved in the TMF on the shared drive and printed, by adding it to the TMF/ISF index. After filing in the paper TMF the TMSO/ATM should ensure the TMF/ISF checklist is updated.

2.4.11 Study correspondence sections do not need to be itemised in the TMF checklist unless there are very few documents in the section and the study team would find it useful.

2.4.12 A list of all the CVs/GCP certificates does not have to be added to the TMF/ISF index, a file note can be added indicating that the details will be held in a separate CV/GCP tracker in the study specific folder in Section 6.

2.4.13 Empty sections or incomplete documentation should be explained with a file note.

2.4.14 Throughout the study the TMSO/ATM should complete a quality check of the documents that are being filed. For example, check that CVs are signed and dated before filing, and ensure that printed documents are legible and complete.

2.4.15 Throughout the study the TMSO/ATM should keep the TM informed of any issues with the TMF/ISF and should query any filing that is unclear.

2.4.15 Where the TM team is to be blinded to study allocation/intervention, ensure that information relating to this (that could potentially unblind) is stored separate from the main TMF, and not accessible to the TM team during the trial.

## **2.5 Procedure – Review**

The trial management team will review the TMF on a regular basis to ensure it is up to date. A full review should be completed at least once a year.

First, ensure the TMF & ISF Index itemises all the documents saved in the TMF in the study folder on the shared drive. Update the TMF & ISF Index checklist with any documents that are missing. To simplify the process the reviewer can look on the drive to see what documents or files have been added/modified since the previous review. The date of the previous review will be documented in the file review tracker, stored in TMF section 0.1.

Then the paper TMF will be checked against the up to date excel index. Any missing documents will be printed, filed and the index will be updated. Sections with missing document(s) or empty sections should be brought to the attention of the TM. A file note may be required to explain the empty section.

Once the TMF review is completed the details should be recorded on the review tab of the TMF & ISF Index. This should be printed off, signed and dated and filed in section 0.1 of the TMF.

The TMSO/ATM should on a regular basis review the ISF checklist and follow up with sites to (1) obtain any missing site-customised documents, or (2) to obtain confirmation certain

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documents have been filed in the ISF, or (3) send the sites documents they are missing in the ISF.

A full ISF review will be carried out by the site team as part of site close down but can be done at any time during the study and may be useful prior to a monitoring visit.

## 2.6 Archiving

Archiving of paper TMF and electronic documents should be carried out as described in ACCORD SOPs CR009: Study Closure and Archiving and GS005 Archiving Essential Study Documentation. When archiving electronic documents care must be taken to ensure:

- The electronic documents cannot be altered, i.e. read access only;
- If documents are transferred to electronic storage media for archiving, they should be checked for accuracy and completeness after transfer;
- Consideration should be given to the type of electronic storage media used. If there is a risk the media will become obsolete during the archiving period another type of storage media should be used.

## 3. RELEVANT DOCUMENTS AND REFERENCES

Add a list of relevant SOPs, templates, documents or website links that relate to this SOP.  
ACCORD: [SOPs | Accord](#)

- ACCORD Document Checklist CTIMP CR001-T01
- ACCORD Document Checklist non-CTIMP CR001-T02
- ACCORD Document Checklist Medical Device CR001-T03
- ACCORD Study Closure and Archiving CR009
- ACCORD Archiving Essential Study Documentation GS005
- <https://www.accord.scot/research-access/resources-researchers/sop>

ECTU:

- [ECTU SOP TM 20 Provision of ISFs to Study Sites](#)
- [TM-T2 TMF ISF Index Template](#)
- [TM001 - Non-CTIMP ISF Table of Contents Template](#)
- [TM002 - CTIMP ISF Table of Contents Template](#)

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