

# Tabel of Contents Trial Master File (TMF)

Clinical trial CTR English

**Detta dokument är framtaget och kvalitetssäkrat av Kliniska Studier Sverige.**

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Stödet vi erbjuder ger goda förutsättningar för kliniska studier av hög kvalitet.

## **Trial Master File (TMF)**

*This template is adjusted to follow the EU regulation* *on clinical trials on medicinal products for human use 536/2014 and that the application is made through the EU portal CTIS (Clinical Trial Information System).*

*Note that this template might be updated within shortly as the interpretation of the regulation becomes clearer.*

The Trial Master File (TMF) is the sponsor’s folder and contains all essential documents for the current clinical trial. Contents of a TMF are described in chapter 8 of the ICH-GCP E6 guidelines, with the reservation that the index must be adapted to a particular clinical trial (e.g., more or fewer essential documents can be required to be able to reconstruct a clinical trial), since not all sections are applicable for all types of studies. Chapter 8 describes which documents should be available before, during and after completion of a clinical trial. A blank table of contents page can be found on the last page of this document.

Several documents should be available both in the Investigator Site File (ISF) and in the TMF at the sponsor. According to ICH-GCP, CRF (case report form) originals should be stored at the sponsor and a copy at the investigator after the clinical trial is completed. For other documents, ICH-GCP does not specify where the original or copy should to be stored. A common recommendation is that the document is saved in original where it was created.

It is the sponsor’s responsibility to:

* keep the TMF complete and updated during the ongoing clinical trial
* store the TMF in a safe way while the clinical trial is ongoing and during the retention time
* ensure that archiving occurs in accordance with current legislation
* provide a reference if any document is stored elsewhere than in the TMF.

**Version 26Jan2022** is updated according to EU CTR:

* section 6 and 7 is combined to one, Regulatory information to medical agency within EU; application and approvals
* new section with Reported serious breaches and reported other events of importance.

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| **Index for TMF** | | **Contents:** | **Comments:**  *Help text (in Italics) column to be removed when using the index* |
|  | **Clinical trial team** | * Address and telephone list | *Contact information for important parties such as the sponsor, clinical trial management, site personnel, monitors, external parties e.g., laboratories.* |
|  | **Signed protocol and amendment(s)** | * Approved, signed protocol incl. attachments * Approved, signed amendment(s) * Signed protocol pages and amendment(s) for all responsible investigator(s) * Superseded versions[[1]](#footnote-1)1 | *The signature page should include signatures from the sponsor and coordinating investigator and/or responsible investigator(s).* |
|  | **Case Report Form (CRF/eCRF)**  **Subject Questionnaire**  **Diary** | * CRF/printed version of eCRF (template) * CRF access and training log * CRF completion guidelines * Subject Questionnaires (template) * Diary (template) * Superseded versions1 * Annotated CRF   **At trial end**   * CRF data; paper (original) or electronic * Data Clarification Form (DCF); paper (original) or electronic |  |
|  | **Data Management** | * Data Management Plan * Clean File Form * Database lock * Critical Error Form (if relevant)\* | \*Critical Error Form. *To be used if the database is locked but a critical error that can affect analyses is discovered, and the database thus needs to be unlocked. Document the reason why the database was unlocked and actions required before the database was re-locked.* |
|  | **Subject Information and Informed Consent Form** | * Current Subject Information and Informed Consent Form. Original and translated version(s) if relevant * Other written information provided to participants (e.g., advertisements, diaries, Patient ID card/emergency card, questionnaires) * Superseded approved versions if changes have been made[[2]](#footnote-2)2 | *Signed consent shall only be stored at the site.* |
|  | **Regulatory information to medical agency in EU; Applications and approvals** | * Application, including cover letter and required documents to CTIS\* part I and II[[3]](#footnote-3)3 * Modifications, including cover letter and required documents to CITES part I and II3 * Approvals, dated (initial and for any modifications). * Related correspondence, e.g., yearly safety reports (ASR) | *(CTIS=EMA Clinical trials information system)* |
|  | **Other applications, notifications and registrations** | * Biobank incl. application, application(s) for amendment, approval(s). MTAs[[4]](#footnote-4)4 and correspondence * Notification/registration in accordance with GDPR. Incl. ap plication, application(s) for amendment and correspondence * Registration to public database (if applicable) | *Site’s local biobank applications are stored only in the ISF.* |
|  | **Contracts/agreements and financial aspects** | Financial contracts/agreements, such as   * Sponsor, co-sponsors and CRO * Sponsor and site/Investigator * CRO and site/Investigator * Investigator/institution and authority (if applicable) * Pharmacy agreement (if applicable) * Laboratories agreement * Monitoring agreement * Other agreements * Data Processing Agreement * Budget and financial accounting/documentation |  |
|  | **Site personnel; delegations and CVs** | * Signature and delegation list, signed. Copies from all local sites at trial end * CV for responsible Investigator, sub-Investigators as well as other personnel who are delegated tasks in the trial with documentation regarding GCP training (signed, dated) * CV monitor * CV other relevant personal if applicable, such as laboratory, X-ray personnel |  |
|  | **Investigational Product, product description** | * Current Investigator’s Brochure (IB)[[5]](#footnote-5)5 or SPC, for all included investigational products * IB superseded versions[[6]](#footnote-6)6 * IB shipping receipt for all sites * Disclosure of what is used as reference safety information (RSI) * Safety updates (not ASR nor SUSAR) | *Separate rows can be used if there are several investigational products.* |
|  | **Investigational medicinal Product and Auxiliary medicinal product\*\*, handling** | * Labeling of Investigational Product * Certificate of Analysis, GMP certificate, QP[[7]](#footnote-7)7 release * Shipping documents (to all pharmacies/sites) * Ordering instructions * Requisitions * Investigational product log (inventory log and / or drug accountability log per site or per subject). Template/-s and completed documents from participating centers at the end of the trial\*\* * Instructions for handling investigational product and trial-related material\*\*\* * Temperature log, template * Destruction form, template as well as completed forms from participating centers at the end of the trial * Documentation of investigational product destruction/ receipt from the organization that destructed the investigational product. * Related correspondence | *List if any documents are stored at, e.g., the pharmacy.*  *\*Auxiliary medicinal product with no marketing authorization*  *\*\*Documentation of investigational products must be available.*  *Depending on the trial, it can be a single log or several different logs.*  *\*\*\*if this is not included in the protocol or IB* |
|  | **Randomization and decoding** | * Randomization procedure * Randomization list (if relevant) * Instructions for emergency decoding * List of code-break envelopes (if relevant) | *Documentation of code-breaking is done at the end of the trial, including which envelopes were used and which were not used.* |
|  | **Laboratory information** | * List of laboratories * List of reference ranges from local and external labs, incl updates * Accreditation or certification * Method description for all analyses which lacks accreditation * Instructions for sampling, handling, and storage * Temperature log (copy) | *Local, e.g., for routine samples.*  *External for non-routine samples*. |
|  | **Examinations, measurements** | * Instructions * Referrals/forms * Validation of equipment * Certificates |  |
|  | **Source data** | * Source data verification document, template | *Initial copy as well as an updated copy at end of the trial.* |
|  | **Screening log** | * Screening log (if applicable) | *If needed copy from all sites at end of the trial or otherwise only originals in ISF.* |
|  | **Monitoring** | * Current monitoring plan, as well as superseded versions * Monitoring log (template)*\** * If applicable, Confidentiality agreement*\** * Correspondence | *\* Not a regulatory requirement that these documents should be collected from participating centers* |
|  | **Monitoring reports** | * Documentation from planning meeting, Investigator meeting(s) * Site initiation visit report from all local sites * Monitoring reports from all local sites * Report from close-out meeting from all local sites, as well as national close-out report * Related correspondence |  |
|  | **Reporting of incidents/adverse medical events (AE, SAE and SUSAR) and Annual safety reports** | * Instructions for AE, SAE and SUSAR reporting, incl. reporting forms * Reported SAE for all local sites * Reported SUSARs in the trial * Opinion from DSMB * Annual safety reports (ASR) |  |
|  | **Serious Breaches and other reported events for subject safety** | * Reported serious breaches * Other reported events relevant for subject safety |  |
|  | **Note to File** | * Note to files for all local sites * List of incidents/protocol deviation log from all sites\* * GCP deviations and clarifications | \**Copy at trial completion* |
|  | **Correspondence** | * Relevant communication for the clinical trial (emails, letters, phone contact reports, etc.) * Reports from Investigator meetings * Newsletter |  |
|  | **Reports** | * Clinical trial report * Public summary * Statistical report |  |
|  | **Archiving** | * Archive list including location |  |
|  | **Other** | * Insurance(s) * Audit certificate/inspection report |  |

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1. 1 Superseded versions to be stored here or in another folder. If another folder is used, there might be a reference in the index to where superseded documents are stored. Mark superseded documents “Inactive” to avoid accidental use. [↑](#footnote-ref-1)
2. 2 Superseded versions to be stored here or in another folder. If another folder is used, there must be a reference in the index about where superseded documents are stored. Please mark superseded documents “Inactive” to avoid accidental use [↑](#footnote-ref-2)
3. 3 Should be versioned controlled [↑](#footnote-ref-3)
4. 4 Material Transfer Agreement [↑](#footnote-ref-4)
5. 5 Investigator’s Brochure can be stored separately from the TMF, e.g., electronically, in which case the location should be documented [↑](#footnote-ref-5)
6. 6 Superseded versions to be stored here or in another folder. If another folder is used, there must be a reference in the index about where superseded documents are stored. Please mark superseded documents “Inactive” to avoid accidental use [↑](#footnote-ref-6)
7. 7 Qualified Person [↑](#footnote-ref-7)