Category: Study Procedures

Title: Preparation of trial master file (TMF) for clinical trials

SOP No. : DCP/Ph1/020

Date first effective: 01 Jan 2025 **Review date: 31 Dec 2025**

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SOP No.: DCP/Ph1/020 **Total pages:** 15

Date first effective: 01 Jan 2025 **Next Review date:** 31 Dec 2025

Version: 02

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DCP/Ph1/020: Preparation of trial master file for clinical trials

1. Purpose: The purpose of this SOP is to describe the procedures for preparing and maintaining the Trial Master File (TMF) for clinical trials

2. Scope: This SOP is limited to preparing and maintaining the TMF at our institute.

3. Responsibilities: The responsibilities for ensuring implementation of this SOP lies with the Principal Investigator (PI).

4. Applicable rules, regulations and guidelines:

- Ethical Guidelines for Biomedical and Health Research involving Human Participants, ICMR (2017)
- International Council on Harmonization (ICH); Good Clinical Practice Draft Guidelines: (R3) dated 19th May, 2023.
- Medical Devices Rules, India, 2017
- New Drugs and Clinical Trials Rules, 2019

5. References (to other SOPs)

- None

6. Detailed instructions

S.No	Task	Person responsible
1	Select a file for the TMF	Study co-ordinator
2	Label the TMF with the following: • Study title • Institutional Ethics Committee (IEC) protocol number • Name of sponsor	PI / Co-I / Study co-ordinator

	• Name and affiliation of PI • Date of regulatory approval (if applicable) • Date of IEC approval	
3	Prepare the first page of the TMF as follows: • Title of the study, Name of Study Team • IEC Protocol number • CTRI registration number • Date of Licensing authority approval (if applicable) • Name of the Principal Investigator • Date of the initial protocol submission • Date of the IEC approval • Date of the Site Initiation Visit (SIV) • Total sample size • No. of participants approved for this site • Date on which the first participant was enrolled • Date of last participant's last follow up (updated accordingly) • Date of submission of the annual study report • Date of study close out visit by the sponsor (updated accordingly) • Date of close out report submitted to the IEC (updated accordingly) • Date of submission of Clinical Study Report (CSR) to IEC • Date of archival of the documents	PI / Co-I / Study co-ordinator

4	Prepare the subsequent contents of the TMF as given in Appendix 1	PI / Co-I / Study co-ordinator
5	Maintain the TMF in a secure locker / cupboard	Study co-ordinator
6	Update the TMF in real time as new documents are generated / become available	PI / Co-I / Study co-ordinator
6	Review the TMF once a month for completion. If not complete, then take appropriate steps for completion	PI / Co-I

Note:

- Maintain the TMFs in a legible condition and such that it can be easily retrieved upon the request of a regulatory authority and/ or IEC.
- Record any change in the location of the TMF in order to allow tracking.
- Adequate, safe and suitable space should be available for the secure storage of TMFs of completed studies in the archival room for 5 years after the trial is completed or as per the instructions from sponsors/ IEC

7. Abbreviations

AE	Adverse event
Co-I	Co-investigator
CRF	Case Record Form
CRO	Contract Research Organization
CSR	Clinical Study Report
CTRI	Clinical Trials Registry of India
GCP	Good Clinical Practices
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

ICMR	Indian Council of Medical Research
IEC	Institutional Ethics Committee
PI	Principal Investigator
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TMF	Trial Master File

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APPENDIX 1

CHECK LIST OF THE DOCUMENTS FOR A TMF

Before site initiation

SR. No.	Title of Document	Purpose

6.1.1	Signed protocol and amendments (if any) and sample case record form (CRF)	To document investigator and sponsor agreement to the protocol/amendment(s) and CRF
6.1.2	Information given to trial subject - informed consent document -assent document (if applicable) (including all applicable translations, back translations with translation certificates)	To document the informed consent
6.1.3	Subject diary card/ questionnaire (if applicable) (including all applicable translations, back translations with translation certificates)	To document study related events during follow up
6.1.4	Investigator's brochure	To document that relevant and current scientific information about the investigational product has been provided to the investigator
6.1.5	Advertisement for volunteer recruitment (if used)	To document that recruitment measures are appropriate and not coercive
6.1.6	Financial aspects of the trial, if any	To document the financial agreement between the investigator/institution and the sponsor for the trial
6.1.7	Insurance policy/ certificate (where required)	To document that compensation to participant(s) for trial-related injury will be available

6.1.8	Signed agreement between involved parties, e.g.: - investigator/institution and sponsor - investigator/institution and CRO - sponsor and CRO - investigator / institution and authority(ies) (where required)	To document agreements
6.1.9	Final approval letter (letter of permission) from respective IEC	To document that the trial has been subjected to IEC review and given approval/favorable opinion. To identify the version number and date of the document(s)
6.1.10	Regulatory authority Approval/ notification of protocol (where required)	To document appropriate authorization/ approval/ notification by the regulatory authority has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s)
6.1.11	CTRI registration	To ensure transparency, accountability and internal validity of the study
6.1.12	Administrative approval letter Administrative sanction for sending blood samples outside the institution (if applicable)	To ensure whether administrative sanction has been taken a-priori
6.1.13	Curriculum vital, medical registration certificate and GCP certificate of study team members	To document qualifications and eligibility to conduct trial and/or provide medical supervision of participants
6.1.14	Duty delegation log	To ensure the study related work is performed by the delegated team member
6.1.15	Copy of annexures of initial submission	To ensure whether required documents are submitted for initial IEC review

6.1.16	Letter(s) of communication from IEC	To ensure whether all study related events are reported to IEC
6.1.17	Letter(s) of communication from sponsor (if applicable)	To ensure whether all relevant communications from sponsor are documented
6.1.18	Normal value(s)/ range(s) for medical/ laboratory/ technical procedure(s) and/or test(s) included in the protocol (if applicable)	To document normal values and/or ranges of the tests
6.1.19	Medical/laboratory/ technical procedures/ tests (if applicable) - certification or accreditation or established quality control and/or external quality assessment or other validation (where required)	To document competence of facility to perform required test(s), and support reliability of results
6.1.20	Instructions for handling of investigational product(s) and trial-related materials (if not included in protocol or Investigator's Brochure)	To document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and trial-related materials
6.1.21	Shipping records for investigational product(s) and trial-related materials	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions, and accountability
6.1.22	Certificate(s) of analysis of	To document identity, purity, and strength of investigational product(s) to be used in the

	investigational product(s) shipped	trial
6.1.23	Master randomization list	To document method for randomization of trial population
6.1.24	Decoding procedures for blinded trials [if not mentioned in the protocol]	To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining participants' treatment
6.1.25	Site feasibility report (if applicable)	To document that the site is suitable for the trial
6.1.26	Site initiation visit report (if applicable)	To document that trial procedures were reviewed with the investigator and the investigator's trial staff
6.1.27	Ethics committee registration number [mentioned in IEC communication documents]	
6.1.28	Undertaking from the sponsor [If Applicable]	
6.1.29	IEC approval letter copies of other sites (if applicable)	

6.2. During the conduct of the Trial

SR. NO.	Title of Document	Purpose

6.2.1	Investigator's brochure updates [If any]	To document that investigator is informed in a timely manner of relevant information as it becomes available
6.2.2	Any revision to: - protocol/amendment(s) and CRF - informed consent form - any other written information provided to participants - advertisement for participant recruitment (if used)	To document revisions of these trial related documents that take effect during trial
6.2.3	Dated, documented approval/favorable opinion of institutional ethics committee (IEC) of the following: - protocol amendment(s) - revision(s) of: - Informed consent form - Any other written information to be provided to the participant - Advertisement for participant recruitment (if used) - Any other documents given approval/favorable opinion - Continuing review of trial (where required) Letter of communication from IEC	To document that the amendment(s) and/or revision(s) have been participant to IRB/IEC review and were given approval/favorable opinion. To identify the version number and date of the document(s).
6.2.4	Regulatory authority approvals/ notifications where required for: - protocol amendment(s) and other	To document compliance with applicable regulatory requirements

	documents	
6.2.5	Curriculum vitae for newly added investigator(s) and/ or sub-investigator(s)	
6.2.6	Updated duty delegation log	To ensure the study related work is performed by the delegated team members
6.2.7	Updates to normal value(s)/ range(s) for medical/ laboratory/ technical procedure(s)/ test(s) included in the protocol	To document normal values and ranges that are revised during the trial
6.2.8	Updates of medical/laboratory/ technical procedures/tests - certification or - accreditation or - established quality control and/or external quality assessment or - other validation (where required)	To document that tests, remain adequate throughout the trial period
6.2.9	Documentation of investigational product(s) and trial-related materials shipment	
6.2.10	Certificate(s) of analysis for new batches of investigational products	
6.2.11	Relevant communication from sponsor (if applicable)	To ensure whether all relevant communications from sponsor are documented
6.2.12	Monitoring visit reports	To document site visits by, and findings of, the monitor

6.2.13	Relevant communications other than site visits - letters - meeting notes - notes of telephone calls	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting
6.2.14	Notification by investigator to sponsor of serious adverse events and related reports	Notification by investigator to sponsor of serious adverse events and related reports
6.2.15	Notification by sponsor and/or investigator, where applicable, to regulatory authority and IEC of unexpected serious adverse drug reactions and of other safety information	Notification by sponsor and/or investigator, where applicable, to regulatory authorities and IEC of unexpected serious adverse drug reactions
6.2.16	Notification by sponsor to investigators of safety information	Notification by sponsor to investigators of safety information
6.2.17	Data safety monitoring board reports (if applicable)	
6.2.18	Interim report [if available] and annual reports to IEC and authority	Interim or annual reports provided to IEC and to authority
6.2.19	Participant screening log	To document identification of participants who entered pre-trial screening
6.2.20	Participant identification code list	To document that investigator/institution keeps a confidential list of names of all participants allocated to trial numbers on

		enrolling in the trial. Allows investigator/institution to reveal identity of any participant
6.2.21	Participant enrolment log	To document chronological enrolment of participants by trial number
6.2.22	Investigational products accountability at the site	To document that investigational product(s) have been used according to the protocol
6.2.23	Signature sheet	To document signatures and initials of all persons authorized to make entries and/or corrections on CRFs
6.2.24	Record of retained body fluids/ tissue samples (if applicable)	To document location and identification of retained samples if assays need to be repeated

6.3. <u>After Completion or Termination of the Trial</u>

Sr.No.	Title of Document	Purpose
6.3.1	Investigational product(s) accountability at site	To document that the investigational product(s) have been used according to the protocol. To documents the final accounting of investigational product(s) received at the site, dispensed to participants, returned by the participants, and returned to sponsor
6.3.2	Documentation of investigational product destruction (if applicable)	To document destruction of unused investigational products by sponsor or at site
6.3.3	Completed participant identification code list	To permit identification of all participants enrolled in the trial in case follow-up is required. List should be kept in a confidential manner and for agreed upon

		time
6.3.4	Audit certificate (if applicable)	To document that audit was performed
6.3.5	Final trial close-out monitoring report	To document that all activities required for trial close-out are completed, and copies of essential documents are held in the appropriate files
6.3.6	Treatment allocation and Decoding documentation (if applicable)	Returned to sponsor to document any decoding that may have occurred
6.3.7	Final report by investigator to IEC, and where applicable, to the regulatory authority	To document completion of the trial
6.3.8	Clinical study report	To document results and interpretation of trial