**Trial Master File (TMF)**

The Trial Master File (TMF) is the sponsor’s folder and contains all essential documents for the current study. 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 study (e.g., more or fewer essential documents can be required to be able to reconstruct a study), since not all sections are applicable for all types of studies. A blank table of contents page can be found on the last page of this document.

It is the sponsor’s responsibility to:

- keep the TMF complete and updated during the ongoing study
- store the TMF in a safe way while the study 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.
<table>
<thead>
<tr>
<th>Index for TMF</th>
<th>Contents:</th>
<th>Comments:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Study team</strong></td>
<td>• Address and telephone list</td>
<td>Contact information for important parties such as the sponsor, study management, site personnel, monitors, external parties e.g., laboratories.</td>
</tr>
<tr>
<td><strong>2. Signed protocol and amendment(s)</strong></td>
<td>• Approved, signed protocol incl. attachments &lt;br&gt;• Approved, signed amendment(s) &lt;br&gt;• Signed protocol pages and amendment(s) for all responsible investigator(s) &lt;br&gt;• Superseded versions&lt;sup&gt;1&lt;/sup&gt;</td>
<td>The signature page should include signatures from the sponsor and coordinating investigator and/or responsible investigator(s).</td>
</tr>
<tr>
<td><strong>3. Case Report Form (CRF/eCRF) Subject Questionnaire Diary</strong></td>
<td>• CRF/printed version of eCRF (template) &lt;br&gt;• CRF access and training log &lt;br&gt;• CRF completion guidelines &lt;br&gt;• Subject Questionnaires (template) &lt;br&gt;• Diary (template) &lt;br&gt;• Superseded versions&lt;sup&gt;1&lt;/sup&gt; &lt;br&gt;• Annotated CRF At study end &lt;br&gt;• CRF data; paper (original) or electronic &lt;br&gt;• Data Clarification Form (DCF); paper (original) or electronic</td>
<td></td>
</tr>
<tr>
<td><strong>4. Data Management</strong></td>
<td>• Data Management Plan &lt;br&gt;• Clean File Form &lt;br&gt;• Database lock &lt;br&gt;• Critical Error Form (if relevant)*&lt;sup&gt;1&lt;/sup&gt;</td>
<td>*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.</td>
</tr>
<tr>
<td><strong>5. Subject Information and Informed Consent Form</strong></td>
<td>• Current Subject Information and Informed Consent Form. Original and translated version(s) if relevant &lt;br&gt;• Other written information provided to participants (e.g., advertisements, diaries, Patient ID card/emergency card, questionnaires) &lt;br&gt;• Superseded versions if changes have been made&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Signed consent shall only be stored at the site.</td>
</tr>
<tr>
<td><strong>6. Swedish Medical Products Agency (Läkemedelsverket, LV)</strong></td>
<td>• Application, signed. Incl. cover letter and attachments&lt;sup&gt;2&lt;/sup&gt; &lt;br&gt;• Amendment, signed. Incl. cover letter and attachments&lt;sup&gt;2&lt;/sup&gt; &lt;br&gt;• Approval, dated (initial and for any amendments). &lt;br&gt;• Related correspondence, e.g., yearly safety reports (DSUR), declaration of end of trial (End of Trial Form), as well as final report</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>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.<br><sup>2</sup>Must be versioned controlled.
<table>
<thead>
<tr>
<th>Index for TMF</th>
<th>Contents:</th>
<th>Comments: Help text (in Italics) column to be removed when using the index</th>
</tr>
</thead>
</table>
| 7. Swedish Ethical Review Authority (Etikprövnings-myndigheten, EPM) | - Application, signed. Incl. cover letter and attachments\(^2\). Regarding information on radiation doses  
- Application(s) for amendment, signed. Incl. cover letter and attachments\(^2\) (all in one file)  
- Approval(s), dated (initial and for changes) incl. participants at meeting for approval  
- Related correspondence | Note that information for the EPM about SUSAR and annual safety reporting is a requirement according to Swedish Medical Products Agency statutes (in Swedish: LVFS) but is not required by the EPM. |
| 8. Other applications, notifications and registrations | - Biobank incl. application, application(s) for amendment, approval(s). MTAs\(^3\) and correspondence  
- Notification/registration in accordance with GDPR. Incl. application, application(s) for amendment and correspondence  
- Registration to public database (if applicable) | Site’s local biobank applications are stored only in the ISF. |
| 9. Contracts/agreements and financial aspects | Financial contracts/agreements, such as  
- Sponsor 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 |  |
| 10. Site personnel; delegations and CVs | - Signature and delegation list, signed. Copies from all local sites at study end  
- CV for responsible Investigator, sub-Investigators as well as other personnel who are delegated tasks in the study with documentation regarding GCP training (signed, dated)  
- CV monitor  
- CV other relevant personal if applicable, such as laboratory, X-ray personnel |  |
| 11. Investigational Product, product description | - Current Investigator’s Brochure (IB)\(^4\) or SPC, for all included investigational products  
- IB superseded versions\(^1\)  
- IB shipping receipt for all sites  
- Disclosure of what is used as reference safety information (RSI)  
- Safety updates (not DSUR nor SUSAR) | Separate rows can be used if there are several investigational products. |

---

\(^{1}\) 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  
\(^{2}\) Should be versioned controlled  
\(^{3}\) Material Transfer Agreement  
\(^{4}\) Investigator’s Brochure can be stored separately from the TMF, e.g., electronically, in which case the location should be documented
<table>
<thead>
<tr>
<th>Index for TMF</th>
<th>Contents:</th>
<th>Comments:</th>
</tr>
</thead>
</table>
| **12.** Investigational Product, handling | • Labeling of Investigational Product  
• Certificate of Analysis, GMP certificate, QP² release  
• Shipping documents (to all pharmacies/sites)  
• Ordering instructions  
• Requisitions  
• Drug accountable log template(s)  
• Drug accountability per site and per patient  
• Instructions for handling investigational product and study-related material*  
• Temperature log, template  
• Destruction form, template  
• Documentation of investigational product destruction  
• Related correspondence | List if any documents are stored at, e.g., the pharmacy.  
*if this is not included in the protocol or IB |
| **13.** 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 study, including which envelopes were used and which were not used. |
| **14.** Laboratory information | • List of laboratories  
• List of reference ranges from local and external labs, incl updates  
• Accreditation or certification  
• Method description for all analyses  
• Instructions for sampling, handling, and storage  
• Temperature log (copy) | Local, e.g., for routine samples.  
External for non-routine samples. |
| **15.** Examinations, measurements | • Instructions  
• Referrals/forms  
• Validation of equipment  
• Certificates | Initial copy as well as an updated copy at end of study |
| **16.** Source data | • Source data verification document, template | Copy from all sites at end of study or otherwise only originals in ISF. |
| **17.** Screening log | • Screening log (if applicable) | |
| **18.** Monitoring | • Current monitoring plan, as well as superseded versions  
• Monitoring log (template)  
• Confidentiality agreement (copy)  
• Correspondence | |
| **19.** 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 | |
| **20.** Reporting of incidents/adverse medical events (AE, SAE and SUSAR) | • Instructions for AE, SAE and SUSAR reporting, incl. reporting forms  
• Reported SAE for all local sites  
• Reported SUSARs in the study  
• Opinion from DSMB  
• Annual safety report (ASR or DSUR)⁶ | |

---

⁵ Qualified Person  
⁶ Development Safety Update Report
<table>
<thead>
<tr>
<th>Index for TMF</th>
<th>Contents:</th>
<th>Comments:</th>
</tr>
</thead>
</table>
| **21.** 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 study completion |
| **22.** Correspondence | • Relevant communication for the study (emails, letters, phone contact reports, etc.)  
• Reports from Investigator meetings  
• Newsletter | |
| **23.** Reports | • Study report  
• Statistical report | |
| **24.** Archiving | • Documentation for archiving of study documents  
• Final archiving | |
| **25.** Other | • Insurance(s)  
• Audit certificate/inspection report | |
<table>
<thead>
<tr>
<th>Index for TMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Study team</td>
</tr>
<tr>
<td>2. Signed protocol and amendment(s)</td>
</tr>
</tbody>
</table>
| 3. Case Report Form (CRF/eCRF)  
  Subject Questionnaire  
  Diary               |
| 4. Data Management    |
| 5. Subject Information and Informed Consent Form |
| 6. Swedish Medical Products Agency (Läkemedelsverket, LV) |
| 7. Swedish Ethical Review Authority (Etikprövningsmyndigheten, EPM) |
| 8. Other applications, notifications and registrations |
| 9. Contracts/agreements and financial aspects |
| 10. Site personnel; delegations and CVs |
| 11. Investigational Product, product description |
| 12. Investigational Product, handling |
| 13. Randomization and decoding |
| 14. Laboratory information |
| 15. Examinations, measurements |
| 16. Source data       |
| 17. Screening log     |
| 18. Monitoring        |
| 19. Monitoring reports |
| 20. Reporting of incidents/adverse medical events (AE, SAE and SUSAR) |
| 21. Note to File      |
| 22. Correspondence    |
| 23. Reports           |
| 24. Archiving         |
| 25. Other             |