

# Tabel of Contents Investigator Site File (ISF)

Clinical trial CTR English

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

Vi utvecklar och erbjuder stöd för kliniska studier i hälso- och sjukvården.

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

## Investigator Site File (ISF); a part of the 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 Investigator Site File (ISF) is the site’s file and contains all essential site documents for the current clinical trial. Contents of an ISF are described in chapter 8 of the ICH-GCP E6 guidelines, with the reservation that the index must be adapted to the particular study (e.g., more or fewer essential documents can be required to be able to reconstruct a clinical trial), since all sections are not applicable for all types of studies. Chapter 8 describes which documents should be available before, during and after completion of a clinical trial. The site can choose to adapt the sequence of the sections as needed. 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 originals should be stored at the sponsor and a copy at the investigator when 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 site’s responsibility to:

* keep the ISF complete and updated during the clinical trial conduct
* store the ISF in a safe way while the 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 the ISF.

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.

| **Index for ISF** | **Contents:** | **Comments:***Help text (in Italics) column to be removed when using the index* |
| --- | --- | --- |
|  | **Clinical trial team** | * Address and telephone list
 | *Incl contact information for important parties such as the sponsor, study management, site personnel, monitors, external parties, e.g., laboratories.* |
|  | **Signed protocol and amendment(s)** | * Approved, signed protocol incl. attachments
* Approved, signed amendment(s)
* Superseded versions[[1]](#footnote-1)
 | *The signature page should include signatures from the Sponsor and coordinating investigator (for multi-center trials) and/or responsible investigator.* |
|  | **Case Report Form (CRF/eCRF)** **Subject Questionnaire****Diary** | * CRF/printed version of eCRF (template)
* Subject Questionnaire (template)
* Diary (template)
* CRF completion guidelines
* Working instructions/template (where relevant)
* Superseded versions of CRF and worksheet1

**At trial end*** Copy of CRF data (paper or electronic copy)
* Copy of Data Clarification Form (DCF) (paper or electronic copy)
 |  |
|  | **Subject Information and Informed Consent Form**  | * Current Subject Information and Informed Consent form (template)
* Any other written information provided to the subject(s) (e.g. Patient ID Card/emergency card or instructions)
* Superseded approved versions of Subject Information and Informed Consent form and other written information1
* Signed Subject Information and Informed Consent form (original)
 |  |
|  | **Regulatory information to medicinal agency in EU; Applications and approvals** | * Approval (copy) incl. cover letter for application/list of submitted documents to CITES\* part I and II. Answer from sponsor regarding supplements in the case it concerns the execution of the trial at the site. Applies to the original application and to applications for amendments.
* Correspondence
 | *CTIS=EMA Clinical trials information system* |
|  | **Other applications, notifications and registrations** | * Biobank agreement incl. the application, application(s) for amendment, approval(s), MTAs[[2]](#footnote-2) and correspondence
* Notification of processing of personal data to the Data Protection Officer (if applicable)
* Other
 | *Whether registration of personal data processing (“Anmälan gällande behandling av personuppgifter”) can be done at each site varies because each region has internal routines for this.* |
|  | **Contracts/agreements and financial aspects** | * Financial contract/agreement[[3]](#footnote-3)
* Signed agreement between the sponsor and site/institution3
* Contract/agreement for study implementation3
* Data Processing Agreement (if applicable)
* Pharmacy agreement (if applicable)
* Trial budget, if the site has made its own budget
 |  |
|  | **Site personnel; delegations and CVs** | * Signature and Delegation list
* CV for investigators and other personnel
* Training log
 | *CV should be signed and dated by the personnel at the site. It is beneficial to attach the GCP certificate to the CV or otherwise store in another folder at the site which can be shown on request. The Signature and Delegation list is updated as needed throughout the study and signed by the responsible clinical investigator at end of study.* |
|  | **Investigational Product, product description**  | * Investigators Brochure (IB)[[4]](#footnote-4) or SPC
* Investigator’s receipt of IB
 |  |
|  | **Investigational medicinal Product and Auxiliary medicinal product\*, handling** | * Instructions for handling investigational product
* Right of requisition
* Requisitions of ordered investigational product
* Investigational product log (inventory log and/or drug accountability log per site or per trial subject) \*\*
* Documentation of destruction of the investigational product
* Temperature log (room, freezer/refrigerator if applicable)
 | *\*Auxiliary medicinal product with no marketing authorization**\*\*Documentation of investigational products must be available. Depending on the study, it can be a single log or several different logs.* |
|  | **Randomization and decoding** | * Randomization procedure
* Decoding procedure
* Result of code-breaking (after trial completion)
 |  |
|  | **Laboratory information** | * Reference ranges incl. updates if changes (if applicable)
* Accreditation incl. attachments or CV for relevant personnel
* Laboratory manuals and referrals
* Documentation of sample shipment
* Temperature log for storage (freezer/refrigerator if applicable)
 | *CVs are only needed for non-accredited analyses performed by specialists/research laboratories.* |
|  | **Examinations, measurements** | * Instructions
* Referrals/forms
* Validation of equipment
* Certificates
 |  |
|  | **Source data** | * Overview of where the source data is kept
 | *Signed by the responsible clinical investigator and monitor at initiation. Updated as needed during the trial .* |
|  | **Screening log** | * Screening log (original)
 |  |
|  | **Subject Enrolment and Identification log** | * Subject Enrolment and Identification log
 |  |
|  | **Monitoring (Quality control)** | * Reports from Investigators’ meetings
* Initiation monitoring report
* Follow-up letters/close-out monitoring reports
* Monitoring log
* Secrecy agreement
 | *If the investigator and sponsor are the same person, follow-up letters should be replaced with monitoring reports.* |
|  | **Reporting of incidents/adverse medical events (AE, SAE and SUSAR) and other safety reports** | * Instructions for reporting
* AE, SAE and pregnancy form
* Reported SAE/pregnancies
* CIOMS/SUSAR report (periodic or individual)
* Reported serious breaches
* Other reported events relevant for subject safety
* Output/opinion from DSMB or similar (if applicable)
 | *If reported SAE/pregnancies are recorded in, e.g., the CRF, this should be indicated with a reference to the CRF under this section.* |
|  | **Note to File**  | * Notes to file and clarifications
* List of incidents / Log of protocol deviations
 | *Here, site personnel should document deviations against the protocol, GCP, or similar that have occurred in the trial. They are encouraged to write what occurred plus describe cause and measures taken. Documentation method can vary in different trials.* |
|  | **Correspondence** | * Relevant communication (email, letters, phone contact reports, etc.)
* Newsletters
 | *All essential correspondence shall regularly be printed from email and placed here. Correspondence with, e.g., EPM or LV is preferably stored under those sections.* |
|  | **Reports** | * Clinical trial report (if applicable, otherwise reference to where the report can be found)
* Public summary
 | *It is not an absolute requirement that the study report is included in the ISF, if one chooses not to archive the final report in the ISF this decision should be documented.* |
|  | **Archiving**  | * ISF archival content list including localization
 | *It could be good if a copy of the ISF archival content list remains at the site at archiving so that one can retrieve archived trial documents if needed, e.g., during an inspection.* |
|  | **Other**  | * Template for medical record documentation
* Form for compensation to study participants
* Insurance certificate
* Publications
* Audit/Inspection
 | *These documents are examples of other documents that can be saved in an ISF (not requirements).* |

## Index for Investigator Site File / ISF

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1. Superseded versions should be stored here or in another folder. If another folder is used, there must be a reference in this index to where superseded documents are stored.

Please mark superseded documents “Inactive” to avoid accidental use. [↑](#footnote-ref-1)
2. Material Transfer Agreement [↑](#footnote-ref-2)
3. Financial agreement, investigator agreement, contract/agreement about the implementation, and budget calculations can sometimes be found in another folder. Refer in the index to where these can be found. [↑](#footnote-ref-3)
4. IB can be stored separated from ISF, e.g., electronically. Refer in the index to where it can be found. [↑](#footnote-ref-4)