**Essential Documents for the Conduct of a Clinical Study**

**ICH Section 8**

**8.2 Before the Clinical Phase of the Study Commences**

During this planning stage, before the study formally starts, the following documents should be generated and filed.

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| --- | --- | --- | --- | --- |
| Document Title | | Purpose | Located in Files of | |
|  | | | **Investigator**  **&**  **Institution** | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.2.1 | **Investigator's Brochure** (if applicable) | To document that relevant and current scientific information about the investigational product has been provided to the investigator | X | X |
| 8.2.2 | **Signed protocol and modifications, if any, and sample case report form (CRF)** | To document investigator and sponsor agreement to the protocol / modification (s) and CRF. | X | X |
| 8.2.3 | **Information given to study subject** |  |  |  |
|  | - I**nformed consent form** (including all applicable translations) | To document the informed consent | X | X |
|  | **Any other written information** | To document that subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent | X | X |
|  | **Advertisement for subject recruitment (if used)** | To document that recruitment measures are appropriate and not coercive | X | **Sponsor - Investigator** |
| 8.2.4 | **Financial aspects of the study** | To document the financial agreement between the investigator /institution and the sponsor or sponsor-investigator for the study | X | X |
| 8.2.5 | **Insurance statement** (where required) | To document that compensation to subject(s) for study-related injury will be available | X | X |
| 8.2.6 | **Signed agreement between involved parties, e.g.:** | To document agreements |  |  |
|  | * Investigator /institution and sponsor or sponsor -investigator |  | X | X |
|  | * Investigator/Institution and CRO |  | X | X  (where required) |
|  | * Sponsor or sponsor -investigator and CRO |  | X | X |
|  | * Investigator/ Institution and authority(ies) (where required) |  | X | X |

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| Document Title | | | Purpose | Located in Files of | |
|  | | | | **Investigator**  **&**  **Institution** | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.2.7 | **Dated, documented approval/favourable opinion of Research Ethic Board (REB) /independent ethics Committee (IEC) of the following:**   * Protocol and any modifications * CRF (if applicable) * Informed consent form(s) * Any other written information to be provided to the subject(s)s * Advertisement for subject recruitment (if used) * Subject compensation (if any) * Any other documents given approval/ favourable opinion | To document that the study has been submitted to REB/IEC review and given approval/ favourable opinion. To indicate the version number and date of the document(s). | | X | X |
| 8.2.8 | **Research Ethics Board/ independent ethics Committee composition** | To document that the REB/IEC is constituted in agreement with GCP | | X | X  (where required) |
| 8.2.9 | **Regulatory authority (ies) authorisation/ approval/ notification of protocol** | To document that appropriate authorisation/ approval/ notification by the regulatory authority (ies) has been obtained prior to initiation of the study in compliance with the applicable regulatory requirement(s) | | X  (where required) | X  (where required) |
| 8.2.10 | **Curriculum vitae and/or other relevant documents evidencing qualifications of investigator(s) and sub-investigator(s)** | To document investigators qualifications and eligibility to conduct study and/or their competence to provide medical supervision of subjects | | X | X |
| 8.2.11 | **Normal value(s)/range(s) for medical/ laboratory/ technical procedure(s) and/or test(s) included in the protocol** | To document normal values and/or ranges of the tests | | X | X |
| 8.2.12 | **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 the Investigator/Institution have access to adequate facilities to perform required test(s), and support reliability of results | | X  (where required) | X |

| Document Title | | Purpose | | | Located in Files of | |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | **Investigator**  **&**  **Institution** | | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.2.13 | **Sample of label (s) attached to investigational product container(s) (where required)** | | To document compliance with applicable labelling regulations and appropriate instructions were provided to the subjects |  | | X |
| 8.2.14 | **Instructions for handling of investigational product (s) and study-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 study-related materials | X | | X |
| 8.2.15 | **Shipping records for investigational product(s) and study-related materials (where required)** | | To document shipment dates, batch numbers and method of shipment of investigational product(s) and study-related materials. Allows tracking of product batch, review of shipping conditions, and accountability | X | | X |
| 8.2.16 | **Analysis certificate (s) of shipped investigational product(s) (where required)** | | To document identity, purity, and strength of investigational product(s) to be used in the study |  | | X |
| 8.2.17 | **Decoding procedures for blinded studies (where required)** | | To document how, in case of an emergency, identity of investigational product can be revealed without exposing the treatment to the remaining participating subjects. | X | | X  (third party if applicable) |
| 8.2.18 | **Master randomisation list (where required)** | | To document method for randomisation of study population |  | | X  (third party if applicable) |
| 8.2.19 | **Pre-study monitoring report** | | To document that the site is suitable for the study (may be combined with 8.2.20) |  | | X |
| 8.2.20 | **Study initiation monitoring report** | | To document that study procedures were reviewed with the investigator and the investigator's study staff ( may be combined with 8.2.19) | X | | X |

* 1. **During the Clinical Conduct of the Study**

In addition to having on file the above documents, the following should be added to the files during the study as evidence that all new relevant information is documented as it becomes available

| **Document Title** | | **Purpose** | | **Located in Files of** | |
| --- | --- | --- | --- | --- | --- |
|  | | | | **Investigator**  **&**  **Institution** | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.3.1 | **Investigator's brochure updates (if required)** | | To document that investigator is informed in a timely manner of relevant information as it becomes available | X | X |
| 8.3.2 | **Any revision to:**   * Protocol/modifications(s) and CRF * Informed consent form * Any other written information provided to subjects * Advertisement for subject recruitment (if used) | | To document revisions of these study related documents given effect during the study | X | X |
| 8.3.3 | **Dated, documented approval/ favourable opinion of institutional review board (REB)/ independent ethics Committee (IEC) of the following:**   * Protocol modification (s) * Revision (s) of:   + Informed consent form   + Any other written information to be provided to the subjects   + Advertisement for subject recruitment (if used)   + Any other documents given approval /favourable opinion   + Continuing review of study (where required) | | To document that the modification (s) and/or revision (s) have been submitted to REB/IEC review and were given approval/favourable opinion. To identify the version number and date of the document(s). | X | X |
| 8.3.4 | **Regulatory authority (ies) authorisations/ approvals/ notifications where required for:**   * Protocol modification (s) and other documents | | To document compliance with applicable regulatory requirements | X  **(where required)** | X |
| 8.3.5 | **Curriculum vitae for new investigator(s) and/or sub- investigator(s)** | | (See 8.2.10) | X | X |

| **Document Title** | | **Purpose** | | **Located in Files of** | | |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | **Investigator**  **&**  **Institution** | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.3.6 | **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 study (see 8.2.11) | | X | X |
| 8.3.7 | **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 study period (see 8.2.12) | | X  **(where required)** | X |
| 8.3.8 | **Documentation of investigational product(s) and study-related materials shipment** | | (See 8.2.15) | | X | X |
| 8.3.9 | **Certificate (s) of analysis for new batches of investigational products** | | (See 8.2.16) | |  | X |
| 8.3.10 | **Monitoring visit reports** | | To document site visits by, and findings of, the monitor | |  | X |
| 8.3.11 | **Relevant communications other than site visits:**   * Letters * Meeting notes * Notes of telephone calls | | To document any agreements or significant discussions regarding study administration, protocol violations, study conduct, adverse event (AE) reporting | | X | X |
| 8.3.12 | **Signed informed consent forms** | | To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each subject in study. Also to document direct access permission (see 8.2.3) | | X | Sponsor-Investigator- |
| 8.3.13 | **Source documents** | | To document the existence of the subject and substantiate integrity of collected study data. To include original documents related to the study, medical treatment and subject’s history | | X | Sponsor-Investigator- |

| **Document Title** | | **Purpose** | | | **Located in Files of** | |
| --- | --- | --- | --- | --- | --- | --- |
|  | | | | **Investigator**  **&**  **Institution** | | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.3.14 | **Signed, dated and completed case report forms (CRF)** | | To document that the investigator or authorised member of the investigator's staff confirms the recorded observations. | X  (Copy) | | X  (Original) |
| 8.3.15 | **Documentation of CRF corrections** | | To document all changes/additions or corrections made to CRF after initial data recording. | X  (Copy) | | X  (Original) |
| 8.3.16 | **Notification by originating investigator to sponsor of serious adverse events and related reports** | | Notification by originating investigator to Sponsor/Sponsor-Investigator of serious adverse events and related reports in accordance with Item 4.11 | X | | X |
| 8.3.17 | **Notification by sponsor and/or sponsor-investigator, where applicable, to regulatory authority (ies) and IRB (s)/IEC (s) of unexpected serious adverse drug reactions and of other safety information** | | Notification by sponsor/**sponsor-investigator** and/or investigator, where applicable, to regulatory authorities and REB(s)/IEC(s) of unexpected serious adverse drug reactions in accordance with 5.17 and 4.11.1 and of other safety information in accordance with 5.16.2 and 4.11.2 | X  **(where required)** | | X |
| 8.3.18 | **Notification by sponsor/sponsor-investigator to investigators of safety information** | | Notification by sponsor**/sponsor-investigator** to investigators of safety information in accordance with 5.16.2 | X | | X |
| 8.3.19 | **Interim or annual reports to REB/IEC and authority (ies)** | | Provided interim or annual reports to REB/IEC in accordance with 4.10 and to authority (ies) in accordance with 5.17.3 | X | | X  **(where required)** |
| 8.3.20 | **Subject screening log** | | To document identification of subjects who entered pre-study screening | X | | X  **(where required)** |
| 8.3.21 | **Subject identification code list** | | To document that investigator/institution keeps a confidential list of names of all subjects allocated a study number on enrolling in the study. Allows investigator/ institution to reveal identity of any subject | X | | **Sponsor-Investigator** |
| 8.3.22 | **Subject enrolment log** | | To document chronological enrolment of subjects by study number | X | | **Sponsor-Investigator** |
| 8.3.23 | **Investigational products accountability at the site (if required)** | | To document that investigational product(s) have been used according to the protocol | X | | X |
| 8.3.24 | **Signature sheet** | | To document signatures and initials of all persons authorised to make entries and/or corrections on CRFs | X | | X |
| 8.3.25 | **Record of retained body fluids/ tissue samples (if any)** | | To document location and identification of retained samples if tests need to be repeated | X | | X |

**8.4 After Completion or Termination of the Study**

After completion or termination of the study, all documents identified in sections 8.2 and 8.3 should be filed together with the following:

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| --- | --- | --- | --- | --- |
| Document Title | | Purpose | Located in Files of | |
|  | | | **Investigator**  **&**  **Institution** | **Sponsor**  **&**  **Sponsor - Investigator** |
| 8.4.1 | **Investigational product (s) accountability at site (if required)** | To document that the investigational product(s) have been used according to the protocol. To document the final accounting of investigational product(s) received at the site, dispensed to subjects, returned by the subjects, and returned to sponsor/**sponsor-investigator.** | X | X |
| 8.4.2 | **Documentation of investigational product destruction (if required)** | To document destruction of unused investigational products by sponsor/**sponsor-investigator** or at site | X  (If discarded at site) | X |
| 8.4.3 | **Complete subject identification code list** | To permit identification of all subjects enrolled in the study in case follow-up is required. List should be kept in a confidential manner and for an agreed upon time | X | Sponsor - Investigator |
| 8.4.4 | **Audit certificate (if available)** | To document that an audit was performed |  | X |
| 8.4.5 | **Study close-out final monitoring report** | To document that the study close-out went according to prescribed requirements, and copies of essential documents are held in the appropriate files |  | X |
| 8.4.6 | **Treatment allocation and decoding documentation (if required)** | Document sponsor with any **treatment** decoding that may have occurred |  | X |
| 8.4.7 | **Final report by investigator to REB/IEC where required, and where applicable, to the regulatory authority (ies) (if required)** | To document study completion | X |  |
| 8.4.8 | **Clinical study report** | To document results and data study interpretation | X  (If required) | X |