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Annex 7

Guidelines for the preparation of a contract research organization master file

Background

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Background

A contract research organization master file (CROMF) is a document prepared by the contract research organization (CRO) containing specific and factual information about the CRO and the conduct of clinical studies as well as the analyses of samples and related operations (including clinical trials, clinical data management, pharmacokinetics and statistical analysis and regulatory affairs) carried out at the named site. If only some of the operations referred to below are carried out at the site, the master file (MF) needs to be presented only for those operations.

In a case where a CRO is responsible for activities pertaining only to bioanalytical procedures, then only sections in the CROMF relating to these should be described. Other sections may be marked as "not applicable".

Where a CRO performs various activities, separate sections could be prepared for the different units, e.g. clinical pharmacology unit (CPU) and bioanalytical laboratory (BAL).

A CROMF provides information on the policies, approach and general activities of a CRO. It is not trial-specific as trial-specific data are submitted in a product dossier. It serves as general information to regulators and can be used during preparation for inspections by regulatory inspectors in addition to the trial-specific data and information submitted for assessment. It also provides an overview of the organization's approach to good clinical practices (GCP), good laboratory practices (GLP) and other guidelines pertaining to its activities.

A CROMF should be submitted to the national medicines regulatory authority (NMRA) where such a document is requested. It should be succinct and as far as possible not exceed 25 A4 pages (where appropriate, supportive documentation may be appended).

An updated CROMF should be submitted when requested by the NMRA, or if significant changes have been implemented by the CRO.

1. General information

1.1 Name and exact address of the CRO, including telephone, fax, 24-hour telephone numbers and e-mail address

1.2 Short description of the CRO (including size, location, number of beds, layout and plan, areas for handling samples and waste)

1.3 Activities as licensed/authorized by the national authority

1.4 Inspections and approvals

1.4.1 Inspections/approvals/accreditations by any regulatory agency

1.4.2 Audits of subcontractors

1.5 Type of studies (and indications, where appropriate) performed on site (a list of projects conducted at this site may be provided)

1.6 Provisions for insurance

1.6.1 Number of employees engaged in studies, quality, storage and distribution

1.7 Contract services employed

1.7.1 Use of outside scientific, analytical or other technical assistance in relation to studies and analysis (e.g. clinical laboratory, bioanalytical laboratory, X-ray facilities and caterers)

1.7.2 Services outsourced, e.g. contracts with tertiary care hospital for handling of medical emergencies, ambulance facility, nutrition, biomedical waste, chemical waste, caterers, pest control and pathology laboratory

2. Quality management system of the contract research organization

(Short description including, e.g. responsibilities of the quality assurance unit. A list of quality system documents can be included)

2.1 Organization chart including the arrangements for quality assurance

2.2 Internal audits and self inspection

2.3 Corrective and preventive action plans (CAPA)

3. Personnel

(A brief description can be presented in tabular format)

3.1 Qualifications, experience and responsibilities of key personnel as applicable

3.1.1 project manager

3.1.2 principal investigator

3.1.3 analytical investigator

3.1.4 biostatistician

3.1.5 clinical research associates

3.1.6 data manager

3.1.7 monitor

3.1.8 the study director(s)

3.1.9 person responsible for quality assurance

3.2 Training of personnel:

3.2.1 training policy and procedure (brief description)

3.2.2 training records

4. Ethics committee

4.1 Constitution and relation to CRO

4.2 Procedures including review and approval of protocols

5. Computer systems

(Short description)

5.1 Hardware

5.2 Software (and version number) used (e.g. in the bioanalytical laboratory, in pharmacokinetic and statistical analysis) and change control procedure

5.3 Data management systems (include a procedural flow chart and a brief description of query generation and resolution)

5.4. Security procedures

5.5 Electronic exchange of confidential information

5.6 Brief description of validation programme

5.7 Back-up and storage of electronic data

6. Equipment and instruments

6.1 Brief description of major equipment and instruments (a list of equipment is not required)

6.2 Qualification, maintenance and calibration programme, including the temperature recording systems

7. Documentation

7.1 Briefly describe document management systems

7.2 Project work flow including quality assurance and control process

7.3 Preparation of protocols

7.4 Preparation of informed consent forms and subject information forms

7.5 Preparation of report forms

7.6 Preparation of final report

8. Safety monitoring

(Brief description)

Adverse drug reaction reporting procedure

Provisions made for emergencies, including protocols and equipment available

9. Investigational medicinal products and comparator products

(Brief description)

9.1 Acquisition, storage, handling, sampling and disposal

9.2 Pharmacy and dispensing

10. Pathology

10.1 Biological sample collection and storage

10.2 Handling and analysis of biological samples

11. Bioanalytical laboratory

(Brief description)

11.1 Method development and validation

11.2 Reference standard materials used for preparation of calibration standards and quality control samples

11.3 Biological matrix storage, and handling of matrix samples

11.4 Analysis of unknown samples

11.5 Preparation and labelling of reagents

11.6 Storage of samples

11.7 Stability procedures

11.8 Waste management

12. Biostatistics

12.1 Data processing and analysis

12.2 Data management

13. Study volunteers

13.1 Procedure for recruitment

13.2 Collecting information on volunteers (e.g. databank), while confidentiality is maintained

13.3 Procedure for obtaining informed consent

14. Other information

14.1 Power supply system — uninterrupted power supply and generator availability and capacity

14.2 Brief description of any other activities performed on site by the CRO

14.3 Any other information which the CRO may feel it appropriate to add