30th PREMA ANNIVERSARY

Tools for Conducting a Clinical Trial

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Protocol

A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.

The protocol usually also gives the background and rationale for the trial, but this could be provided in other protocol referenced documents.

Through out the ICH GCP guide line, the term protocol refers to protocol and protocol amendments.

The protocol contents

- General information
- Background information
- Trial objectives and purpose
- Trial design
- Selection and withdrawal of subjects
- Treatment of subjects
- Assessment of Efficacy
- Assessment of Safety
- Statistics
- Direct access to Source data/documents*
- QC/QA
- Ethics
- Data Handling and Recordkeeping
- Financing and Insurance*
- Publication policy*
- Supplements

* May be addressed in the separate agreement

Protocol

➢Inclusion/ Exclusion	Selection and Withdrawal of subjects
➢Summary of the known potential risk and benefits, if any in human subjects	Background information
➢A specific statement of the primary end points	Trial design
➢A statement that the trial will be conducted in compliance with the protocol, GCP, and applicable regulatory requirements	Background information
➢Efficacy parameter	Assessment of Efficacy

Protocol Adherence

Why?

- **Data will not be clean enough to make a study conclusion**
- **Safety of Subjects will be threatened**

Protocol Adherence

Deviation = Noticeable difference from what is expected or acceptable

- Major deviation
- Minor deviation

Violation = an action that breaks a law, agreement, principle etc.

The Investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB/IEC .....

Except where necessary to eliminate an immediate hazard(s) to trial subjects

As soon as possible, the implement deviation or change, the reasons for it, and if appropriate, the proposed protocol amendment(s) should be submitted.

Case Report form (CRF)

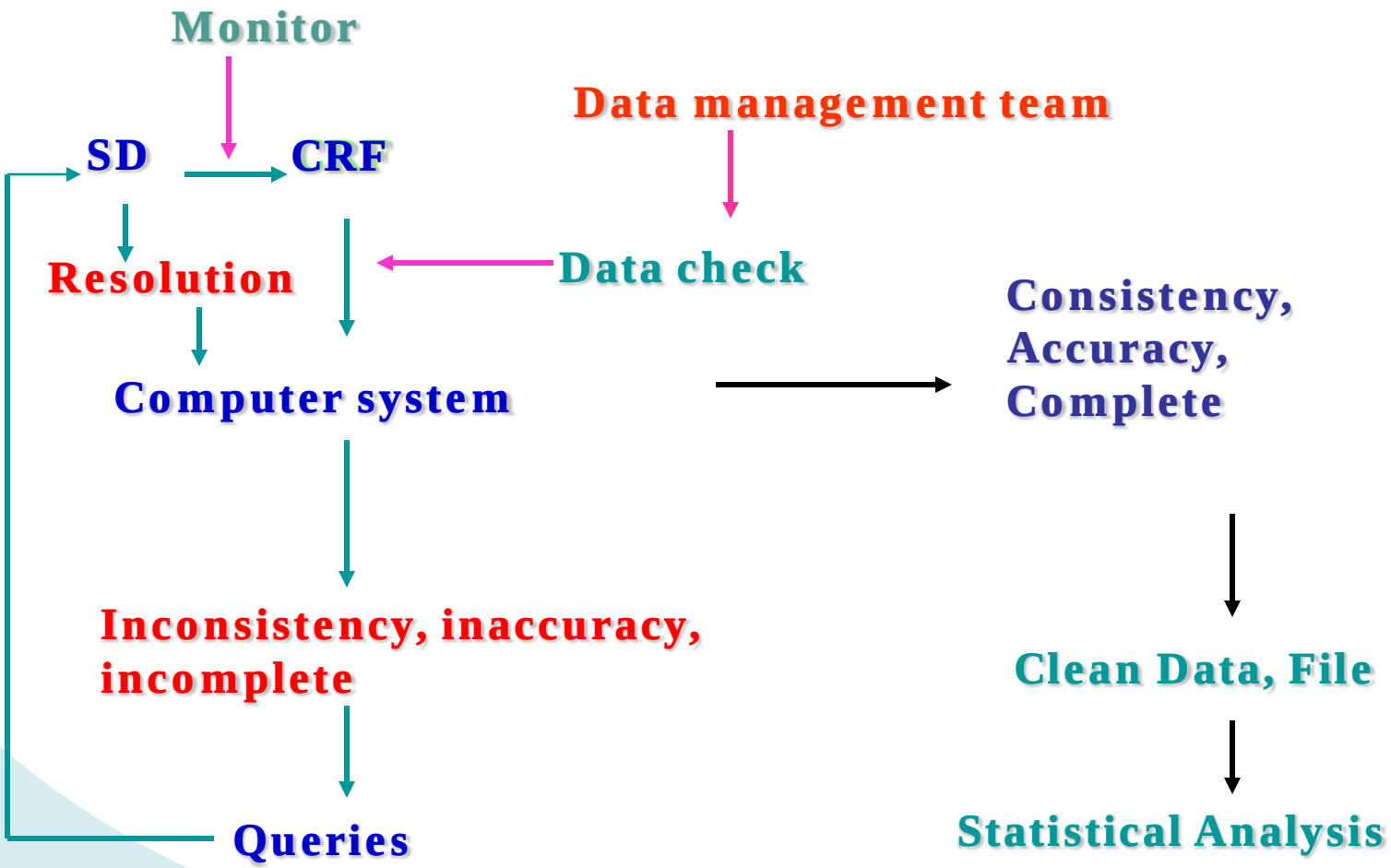
A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject

Source of Documents (SD)

Original documents, data and records

Hospital records, Laboratory notes, X-ray, Pharmacy dispensing record, Copies of laboratory notes, microfilm, Subjects' diaries

Clinical data flow



Records and Reports

The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports

Records and Reports

Any change or correction to a CRF should be dated, initialled and explained (if necessary) and should not obscure the original entry……

The investigator should retain records of the changes and corrections

Completion

Only authorized study staff (names shown in the authorized signatory form, see annex 2) are allowed to enter data into the CRF and other required report forms.

Ballpoint pen must be used.

Capital letters must be used for all entries in the CRF.

All items must be completed by entering a number or text in the space provided.

Completion

When a subject is recruited to the trial, the initial and allocated numbers are entered in the CRF against the subject's name on the subject identification code list. The subject's name should never be entered in the CRF to protect confidentiality.

As far as possible, the results of assessment should first be entered into the subject file and then transcribed into the CRF. This will allow data to be verified during the process of source data verification.

The CRF should be completed during subject participation in the trial.

Data reported on the CRFs that are derived from source documents should be consistent with the source documents or the discrepancies should be explained.

Records and Reports

NM
16/09/04

2001	~~06~~ 05	14
Year	mm	dd

Anticough syrup

Potassium Guiacolsulfonate	300mg
Ammonium chloride	150 ml
Glycyrrhisa extract	0.6ml

NM

Quality assurance (QA) and Quality Control (QC)

1.46 Quality Assurance(QA)

All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s).

1.47 Quality Control(QC)

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial related activities have been fulfilled

Quality assurance (QA) and Quality Control (QC)

5. Sponsor

5.1 Quality assurance and Quality Control

5.1.1 The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOP's to ensure that trial are conducted and data generated, documented (records), and reported in compliance with the, GCP and the regulatory requirement(s)...

5.1.3 QC should be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly

Investigator Brochure (IB)

A compiliation of the clinical and nonclinical data on the investigational product(s) that is relevant to the study of the investigational product(s) in human subjects

.....The IB also provides insight to support the clinical management of the study subjects during the course of the clinical trial

.....The information should be presented.....and non-promotional form that enables a clinician , or potential investigator to understand it and make his/her own unbiased risk benefit assessment of the appropriateness of the proposed trial

Investigator Brochure (IB)

A medically qualified person should generally participate in the editing of an IB, but the contents of the IB should be approved by the disciplines that generated the described data

The IB should be reviewed at least annually and revised as necessary in compliance with a sponsor's written procedure. More frequent revision may be appropriate.....

Sponsor is responsible for ensuring that an up-to-date IB is made available to the investigator(s) and the Investigator(s) are responsible for providing the up-to-date IB to the responsible IRB's/IEC's

Investigator Brochure (IB)

- Table of contents
- Summary
- Introduction
- Physical, chemical and pharmaceutical properties and formulation
- Non-clinical study
  - Non clinical pharmacology
  - Pharmacokinetics and product metabolism in animals
  - Toxicology
- Effects in humans
  - Pharmacokinetics and product metabolism in humans
  - Safety and Efficacy
  - Marketing experience
- Summary of data and guidance for the investigator
- **References on Publications and reports should be found at the end of each chapter**
- Appendices(if any)

Product Insert = Packaging Insert

A document defining information that may be supplied with a pharmaceutical product by the marketing authorization holder

Labels

All finished drug products should be identified by labelling, as required by the national legislation, bearing at least the following information:

the name of the drug product;

a list of the active ingredients (if applicable, with the International Non-proprietary Names (INNs), showing the amount of each present, and a statement of the net contents, e.g. number of dosage units, mass or volume;

the batch number assigned by the manufacturer;

the expiry date in an un-coded form;

any special storage conditions or handling precautions that may be necessary;

the directions for use, and any warnings and precautions that may be necessary;

the name and address of the manufacturer or the company or person responsible for placing the product on the market.

Thank you

PhRMA
Pharmaceutical Research & Manufacturers Association