A V A R E F

GUIDE FOR THE INSPECTION OF CLINICAL TRIALS

DRAFT FOR COMMENTS

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SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT

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Any other follow-up action as required	
Finalization of the Guide	

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1. Background and introduction

To further harmonization in the inspection of clinical trials, the African Vaccines Regulatory Forum (AVAREF) initiated the preparation of a guide for the inspection of clinical trials. This guide, primarily based on World Health Organization (WHO) and other guidelines, is the outcome of a global consultation process. This guide provides for a set of harmonized recommendations for the conduct of an inspection of all phases of clinical trials including bio-equivalence studies (hereafter collectively referred to as clinical trials). Further objectives include to ensure that there is a basis for assuring ethical and scientific integrity of clinical trials, and data integrity. It may be used by inspectors from a National Regulatory Authority (NRA), but may also be used in joint inspections. It can support mutual recognition of inspections of clinical trials between countries that apply the same standards and procedures of inspection. Where relevant, an understanding such as a Mutual Recognition Agreement (MRA) between inspectorates should be considered.

An inspection should cover all aspects, as appropriate, for a clinical trial and as provided for in various WHO Guidelines. Where there are relevant areas for inspection for which WHO has not published a guideline, reference may be made to existing guidelines that should be considered. Areas for the inspection include but are not limited to data and information relating to regulatory approvals, ethics review committee approval, protocols, case report forms (CRFs), clinical trial reports, patient and subject data, sponsors, investigators and personnel involved in the trial, and laboratory data.

This guide can be used to perform an inspection at any stage of a clinical trial. It can also be used after the completion of a clinical trial (once the reports have been submitted to the NRA) to verify that the reports reflect true and accurate data and information. This guide is complemented by an inspection checklist that can be considered during the conduct of an inspection.

2. Scope

This guide covers inspection of clinical trials including bio-equivalence studies. It contains points to review and aspects to verify in areas such as a clinic or Clinical Pharmacology Unit (CPU), the pharmacy and documentation. It includes the review of clinical laboratories and bio-analytical laboratories.

3. Glossary

See AVAREF, WHO and ICH guidelines for the definition of terms used in this guideline.

4. Acronyms

ALCOA	Attributable, Legible, Contemporaneous, Original, Accurate
AVAREF	African Vaccines Regulatory Forum
CAPA	Corrective and Preventive Actions
CIOMS	Council for International Organizations of Medical Sciences
COA	Certificate of Analysis
CPU	Clinical Pharmacology Unit
CRA	Clinical Research Associate
CRF	Case Report Form
CROMF	Contract Research Organization Master File
CRF	case report forms
EC	Ethics Committee
GCP	Good Clinical Practices
GxP	Good Practice
HPLC	High-performance Liquid Chromatography
ICF	Informed Consent Form
ICH	International Council for Harmonization of Technical requirements for Pharmaceuticals for Human use
IP	Investigational Product
LCMSMS	Liquid Chromatography Mass Spectrometry
MRA	Mutual Recognition Agreement
NRA	National Regulatory Authority
WHO	World Health Organization

5. Inspection team

An inspection should be conducted by a team of two or more inspectors who have appropriate qualifications and experience in inspecting clinical trials. The agency responsible for the inspection should appoint the inspection team.

There should be a lead inspector for the inspection, who will be responsible for the co-ordination of the inspection, collation of information from inspection team members, and finalization of the inspection report.

6. Preparation for, and announcement of the inspection

All members of the inspection team should be provided with the relevant information about the scope of the inspection, the site of inspection, and clinical trial(s) to be inspected, to enable them to appropriately prepare for the inspection. Each member of the inspection team should study the relevant, available protocol(s), clinical trial report(s), case report forms, adverse event reports, trial site information and other related documentation. The inspection may be announced. The announcement may be done a few weeks prior to the inspection together with an agenda to be followed. This will ensure the

availability of people at the site and to allow for all the source documents to be retrieved from the archives. The inspection team should decide in advance, who will be responsible for any specific part of the inspection or review of data and information.

7. Conduct of the inspection

The inspectors should present proof of their identity at the start of the inspection. During the opening meeting, inspectors and trial site personnel should introduce themselves. The trial site representatives may give a brief overview of the trial site and the clinical trial to be inspected.

The inspection team should clarify the purpose of the inspection and define the scope of the inspection.

After the introduction, the inspection should be started where the inspectors assess whether the clinical trial was conducted in accordance with all the appropriate GxP guidelines; Declaration of Helsinki; CIOMS guidelines; and the approved protocol. The clinical trial report submitted should be verified against source data.

Data and information to be verified in general, include, but are not limited to:

- licensing requirements for the site conducting clinical trials;
- regulatory requirements and approvals for the conduct of the clinical trials;
- ethics approval;
- the protocol and amendments;
- approvals relating to the protocol and amendments;
- case report forms and raw/source data.

Although clinical trial data and information are still generally recorded on paper, the use of electronic means for generation of data and results, using validated computerized systems, should be encouraged.

8. Data integrity

Decisions made, based on the outcome of clinical trials, rely on the integrity of the results and data obtained during the study. It is important that data and results are reviewed during an inspection, to ensure that the data and information are comprehensive, complete and reliable. The data should be complete, be attributable, legible, contemporaneous, original and accurate, commonly referred to as “ALCOA”. This applies to all data and information as reflected in manual records and electronic data from computerized systems.

9. Protocol

   Clinical trials should be conducted in accordance with the provisions of the study protocol. As the protocol would have been approved prior to the inspection, the following should be verified during the inspection:

   - That the correct protocol, as approved by the NRA (number and version), was followed;
   - That all patients and subjects enrolled, met the inclusion and exclusion criteria;
   - That dosing, meals(fed and fasting), sample collection were done as stipulated;
   - That there is compliance with the requirements such as randomization, product information, reporting of serious adverse events; and preparation of reports;
   - That no deviations occurred that were not approved and justified;
   - That violations to the protocol were reported;
   - That the investigator's signed agreement with the sponsor, confirmation that he or she has read, understood and will work according to the protocol and Good Clinical Practice is available;
   - That reporting of results was done as required.

10. Ethics approval

    The ethics committee (EC) or other board responsible for reviewing the trials ensures the protection of the rights and welfare of human subjects participating in clinical trials. Verify the relevant records relating to the work of the EC, for example:

    - Composition of the EC is in compliance with national requirements (e.g. legislation with regards to the number of people, qualifications, and employment);
    - That the members (chairperson, secretary, members) are free from bias in relation to the clinical trial and sponsor;
    - That the EC operates in accordance with Standard Operating Procedures (SOPs) defining frequency of meetings, notice of meetings, distribution of documents, preparation and distribution of minutes of the meeting;
    - That approval for the clinical trial was given prior to the start of the trial. This is done by reviewing the attendance sheet and minutes of the meeting related to the clinical trial, dates and contents on the letter of approval referring to the protocol, informed consent and related documents (verify numbers, dates, signatures, agenda and minutes of the EC meeting);
    - Approval was given for any advertisement and recruitment of trial subjects, compensation, payments, screening;

- Reports were submitted to the EC as required, as well as reporting of any serious adverse events occurring during the trial.

11. Regulatory approval

All parties involved in a clinical trial should comply with the existing national regulations or requirements. The inspection will consist of a comparison of the procedures and practices of the investigator with those set out in the protocol and reports submitted to the drug regulatory authority. Verify:

- That regulatory approval was granted in writing for the conduct of the trial prior to initiation of the trial. This includes review of the contents of the approval such as date of communication versus trial start date, signature on approval letter, conditions imposed, reference and clinical trial number corresponding, protocol number, informed consent number and version as well as any other information;
- Conditions of approval and responsibilities, and compare with the content of the pre-trial agreement between the sponsor and investigator(s) such as application for approval, amendments to the trial protocol, reporting of all adverse events;
- That any revisions and changes to the protocol and related documents were granted approval prior to implementation;
- Whether serious adverse events and other reports were submitted to the NRA as required.

12. Site

The site should be suitable for the conduct of clinical trials. The different areas should be inspected and assessed against the trial records. In case the site underwent changes since the last inspection, these should be scrutinized.

Verify that the site is licensed (or authorized by another means) to conduct clinical trials in accordance with national legislation. This includes verification of the authenticity of the document issued by the relevant Body in the country of conduct of the trial, referencing the correct address, validity period (issued prior to the trial and valid beyond the trial date), signatures and stamps (as appropriate). This can be verified against the registration of the site, company, organization or business as required in terms of the local legislation.

Verify that the site is in accordance with what is described (e.g. Contract Research Organization Master File (CROMF) or other document). Depending on the activities undertaken by the site, areas such as a clinic or CPU, pharmacy and laboratories should be available with sufficient space, required number of beds, appropriate equipment and instruments, storage for Investigational

Medicinal Products (IMPs) with controlled access and other services as appropriate.

Clinic

The clinic, or clinical pharmacology unit (CPU) should have areas where the different activities relating to the conduct of the trial can be performed. Normally, the following should be available:

- Registration and screening area(s);
- Area for physical examination equipped with the required, calibrated instruments;
- The required number of beds;
- Areas for recreation during stay;
- Areas for dosing, sample collection, sample preparation equipped with the required equipment and instruments such as centrifuges, freezers;
- Equipped kitchen and dining area;
- Emergency room with equipment (e.g. oxygen, defibrillator) and emergency medication as required;
- Emergency medication within their shelf life, with records of stock, administration;
- Toilet facilities.

Pharmacy

There should normally be a pharmacy where IMPs are stored and dispensed under appropriate conditions. Verify:

- That access is controlled and that access records reflect entry and exit against the clinical trial activities (such as dates for receiving and storage of IMPs, dispensing, issuing, returns, and cleaning);
- SOP content for the various activities including receiving, checking, storage, dispensing, labelling and reconciliation of IMPs. Verify the related records to ensure compliance with the protocol and SOPs;
- SOP and records for the monitoring of the conditions under which the IMPs are stored. (Verify the labelling requirements against the room limits and records. The records should reflect the conditions such as temperature and relative humidity observed from calibrated devices. In case there were values that were out of limits, these should have been investigated and the impact on IMPs should have been assessed);
- Records relating to the IMP, such as import license or import authorization, proof of purchase, shipping letter, storage conditions during transport, receipt at the site, COA(s), stock card and dispensing record (dates, quantity, signatures);

- For dispensing, verify the SOP and records for line clearance, preparation of labels, dispensing, signatures and dates for dispensing. (Cross check the records such as label sheets, randomization, CRFs, and reconciliation record for IMPs);
- Whether dispensing was done in the presence of another responsible person e.g. investigator or quality assurance personnel;
- Whether IMP labels contain the correct information such as the study number, "for clinical trial use only", subject number, period, randomization, dosage form, route of administration, as appropriate;
- Whether dosing or administration of IMP was done as required by reviewing the dosing or administration sheet against the CRF, randomization sheet and protocol;
- IMP management record (e.g. "Stock card" or other) by checking the number of dosage units received, quantity dispensed, quantity dosed or administered, quantity returned to stock, quantity on hand, and quantity returned to the sponsor or disposed of;
- SOP for safe disposal of waste.

(Note: Details for the site as described above, can be inspected in detail when data are verified for the clinical trial under inspection, to ensure compliance with the SOPs).

13. Documentation

Quality system

The trial site should have a quality system. The quality system should consist of various documents describing policies, organization, management, responsibilities, formats, contracts, and procedures to be followed including Standard Operating Procedures (SOPs). Documentation should be prepared and controlled with care. The quality system should also cover management of deviations, violations, risk management principles and Corrective and Preventive Actions (CAPA).

The unit responsible for quality assurance should ensure that the quality management system is followed and that the records are maintained.

To assess the quality system, verify for example:

- That the authorized organization chart and job descriptions reflect the reporting lines and responsibilities of personnel for the conduct, control and oversight of the trial(s);
- Curriculum vitae of key personnel are current;
- SOP and records for qualification and training of employees and contracted personnel. Training records should reflect recent and up to date training (which could be internal training and external training);

- Signatures of study personnel (signature list) against the signatures in source documents (e.g. CRFs, dosing sheets).

Contracts

There should be a current, valid contract between the Sponsor and the investigator. (See below).

Where the trial site makes use of contracted staff, such as Clinical Research Associates, (CRAs), nursing staff, custodians, phlebotomists or other personnel, verify that there is a current contract in place, and that the contracted personnel have the required qualifications, experience and training. This can be done by selecting names from the list of contracted personnel, and then verifying the respective records for these personnel.

Archiving

There should be archiving facilities with sufficient space, ensuring the protection of records from damage such as fire, water, humidity and deterioration.

Procedures and records for placement and retrieval of documents and trial data should be available. Verify SOPs and records for the archiving of electronic data and electronic records.

14. Sponsor, investigator and personnel

The contract between the sponsor and the investigator should clearly define the responsibilities of each party. Declarations of interest should be signed and dated. Verify that:

- The contract is valid, i.e. dated, period covering the trial, signatures by all parties, responsibilities indicated including obtaining, transport, storage, use, safe disposal or return of IMPs; monitoring of the trial, quality assurance; reports;
- Scope of insurance (regardless of fault) is defined, provided for and is current;
- Product information was provided by the sponsor in a timely manner.

The sponsor is responsible for providing the investigational product and information, monitoring and compliance with legal, ethical and regulatory principles.

The investigator is responsible to ensure that the conduct of the trial is in compliance with the protocol and requirements. Verify:

- The qualification (degree, as required by national legislation), experience (curriculum vitae) and training records;
- Unbiased selection of subjects (e.g. no preferential selection of family members, friends, staff);
- The signed statement for committing to compliance with GCP and the protocol for the conduct of the trial;
- That full information relating to the IMP was given to the investigator before and during the trial (including e.g. annual update);
- Preparation and signing of the final report was done.

Personnel should have appropriate qualifications, experience and training. Verify that:

- A record reflects delegation of tasks (e.g. in a delegation log);
- A list of signatures is available. Compare the signatures against the source data for the trial being inspected (such as, but not limited to, signatures in training records relating to the trial, recordings in CRFs, dosing charts, sample collection forms);
- The number of employees were appropriate for the conduct of the trial, such as the number of phlebotomists versus the number of subjects and sample collection points;
- Their qualifications, training records and curriculum vitae are available.

15. Monitor(s) and monitoring reports

A sponsor should ensure that the trial site is able to conduct the trial and that the trial is conducted appropriately. A monitor should prepare reports following visits to the trial site.

Verify that the monitoring reports reflect the site review and trial progress. The report should cover review of e.g. compliance with the protocol, data integrity, CRFs, and IMP management.

16. Quality Assurance

Trials should be conducted in compliance with quality assurance principles. Ensure that those who are responsible for the QA review, are independent of the conduct of the trial.

Quality Assurance reports, reflecting the review of the data and information before, during and after the conduct of the trial, should be available.

17. Patients and Subjects

Subjects should be protected from harm in accordance with the principles of GCP, the Declaration of Helsinki and CIOMS guidelines, from the time of recruitment, during participation in the trial and thereafter. Verify that:

- There is an approved procedure for the recruitment, and that the procedure and recruitment materials such as advertisements were approved by the EC. (Note the dates, and version numbers);
- There is an approved procedure for the keeping of records (e.g. electronic or paper) of all subjects and that there is a system to ensure that subjects are not participating in different trials, at the same time, or one trial after the other within a period of time defined in the protocol;
- Subjects are allocated a unique number, in order to ensure identification of each subject, and that the participation in a trial is recorded. (A complete record of participation in studies should be available);
- Vulnerable groups were not included in a trial, unless this is justified;
- Verify source information including proof of the date of birth (such as birth certificate), address, contact details are available;
- In the case of a bio-equivalence study, ensure that there is justification for the number of subjects enrolled in the trial;
- Cross check the signatures of subjects (e.g. receiving payment against the Informed Consent Form (ICF)).

18. Informed Consent Forms (ICFs)

Subjects should be informed of the advantages and disadvantages of participating in a trial. This includes information on the IMP, possible adverse events, insurance and other matters. Verify that:

- There are records reflecting that the required information was presented to the subject, verbally and in writing (informed consent form);
- Each subject signed the ICF prior to participating in the trial, general (where applicable) and trial specific (check dates and signatures);
- ICFs contain all the required information that should be communicated to the subject in a manner and language that the subject understands. These explanations and details should include e.g.
    - aim, benefit, risks, inconveniences when participating in the trial;
    - detail of the IMP to be administered;
    - allowing for voluntary withdrawal from the trial at any time;
    - how remuneration (including pro rata remuneration where necessary) will be done;
    - what the insurance will cover;
    - a statement that information will be kept confidential but may be shared with regulatory authorities;

- provision for access to treatment when needed;
- an explanation that termination can be done by the investigator if needed;

- Correct version of the ICF was signed (or accepted by other means such as a fingerprint) and dated prior to participation in the trial;
- Contact details of PI or secretariat was given to the subjects;
- Provision was made to allow subjects to ask questions relating to the study.

19. Randomization

Trials often have more than one type of treatment. This may require that there is a randomization process to ensure that there is no bias in allocating the type of product(s) to be administered to the subject. Verify that:

- There is a procedure that describes how that randomization should be done. Check that the randomization was done according to the SOP for the trial being inspected. Records should be available reflecting the date, time, software, and version used;
- IMPs were dispensed and dosed to subjects, in accordance with the randomization schedule for the specific trial. (Compare the randomization list against the dispensing sheets, dosing labels, and CRFs).

20. Case Report Forms

Trial related data and information should be recorded in Case Report Forms (CRFs). Verify that:

- The results and data recorded are the same as those reflected in the source documents (such as laboratory reports). In case corrections were made when data were entered, ensure that the results are accurate and reliable, and that the reason for the change was given, signed and dated;
- Samples such as blood and urine were taken, chest X-ray or other tests were done as defined in the protocol, and that the results are within the specified ranges as required. Review the comments made by the investigator in case any result was out of range;
- The protocol was followed where it refers to the trial being conducted under fasting or under fed conditions. Where meals were to be provided, check that these were prepared and served at the correct times, correct caloric content, and that the amount or volumes consumed by each volunteer was recorded;
- Other source data are as recorded in CRFs, such as, but are not limited to:
  - Inclusion and exclusion criteria;
  - Age;
  - Administration of the correct IMP;
  - Sample collection time;
  - Blood pressure values, pulse rate, respiration, temperature;

- Recording of adverse drug events;
- Recording of concomitant medication;
- Recording of the number of samples taken against number of samples transferred for preparation or storage and analysis.

21. Laboratory and analysis

Laboratories should be able to analyse samples as specified in the protocol. When testing is outsourced, contracts should define the responsibilities and scope of each party including sample transport, storage, preparation, methods to be used and reporting of results. Laboratories should operate in compliance with GxP. Review the contracts.

Clinical laboratory

In reviewing data and results from the clinical laboratory, verify that:

- SOPs are followed for supplier qualification and procurement (approved vendor list);
- laboratory staff is competent to perform tests as required;
- procedures and records for the qualification and calibration of the laboratory equipment and instruments are maintained;
- equipment log books are maintained;
- current normal ranges and values of the measures are specified;
- procedures are in place for the receipt, storage and handling of certified reference materials, chemicals and reagents, that no expired stock is used, and that storage conditions are maintained;
- COAs of materials are available;
- Procedures are available for handling hazardous materials e.g. live viruses;
- Environmental monitoring of test areas is done;
- Test methods are verified or validated as appropriate;
- Procedures for retesting as required, are available;
- Printouts of test results comply with ALCOA principles;
- Procedures and records for the safe disposal of the laboratory waste are followed.

Bio-analytical laboratory

The laboratory should have the necessary resources to perform the required analysis. This includes, but is not limited to premises, personnel, equipment, instruments, and documentation. Where licensing is required by national legislation, verify the validity of the license (e.g. name, registration, date, and scope of activities approved).

Ensure that there are respective areas for sample receiving and storage, sample preparation, analysis and other areas as required. Areas should be clean and

maintained, access controlled and that the conditions are as required (e.g. temperature, light, relative humidity) if required.

Verify personnel qualifications, experience and training records.

Verify that the required equipment and instruments are available, qualified and calibrated – including e.g. freezers, balances, centrifuges, pH-meters, micropipettes, HPLCs, LCMSMS.

Inspect the above specifically related to the trial. Review the specific source data for the trial and sample analysis by following the flow of the samples from receipt, to storage, processing, analysis, results, processing and reporting.

Sample management

There should be procedures and records available reflecting the sample transfer from the CPU, and receipt in the BAL. Verify that:

- The details of the procedure and records such as the dates and number of samples transferred to the BAL against the data and information in e.g. CRFs, freezer logs, transfer sheets (number of subjects, periods, number of samples collected and samples processed);
- That the samples were stored at the required temperature (e.g. -20 or -70 degrees Celsius) until analysed. (The storage conditions must be as required by the protocol. Verify the temperature records for the storage period. In case of any excursions, review the investigations and impact analysis;
- Freezers used for storage of samples were qualified. There should be protocols and reports as well as procedures for the installation, operation and performance of the freezers, temperature mapping, source data, and calibration certificates e.g. for sensors;
- Procedures and records for the placement and withdrawal of samples are accurate.

Equipment and instruments

Note the identification and reference numbers of instruments reflected in the report and source data reports, and then verify the records for those instruments and equipment. For example, balances, pipettes, micro-pipettes, HPLC, and LCMSMS – verify that the qualification and calibration status was valid at the time of use for method validation as well as sample analyses for those used for the trial.

Method of analysis

The method used for the analysis of samples, should be a validated method. For example, in the case of blood plasma samples, review the bio-analytical method

used for sample analysis and ensure that the method was validated before it was used to analyse the samples. Review the following:

- Method development: Procedure, literature study, records;
- Method validation: Procedure and records for all parameters, including full validation, partial validation and cross validation. Review the raw data against the report, including electronic results (such as chromatograms) for authenticity, audit trail, date, changes, and data integrity;
- Sample and solution stability procedures and records;
- Reference materials used: Certificate of analysis, usage record, batch number used against data, expiry date, weights, preparation of solutions, dilutions and calculations.

Sample analysis

Verify the data reflected in reports against the source data. Ensure that all the samples for the number of subjects were analysed (compare number of subjects enrolled in the trial, all the periods, sampling times, samples transferred from CPU to BAL, samples prepared, back- up samples) and select results from the report for verification against electronic data. For electronic data verification, verify at least the following:

- Ensure that the instrument used (e.g. HPLC, LCMSMS) was in a qualified and calibrated state at the time of sample analysis;
- Select records (printed) of data such as chromatograms, and verify these against the electronic data for the sample set. Verify the date of analysis, time, analyst identification, system audit trail, changes, peak areas, integration and other related information for accuracy and reliability (ALCOA+);
- Verify that the sample set met the requirements (e.g. calibration curve, Quality control samples);
- Check whether there was any repeat analysis, and whether this was done in accordance with the SOP;
- Ensure that Incurred Sample Analysis was done according the SOP and that the results were acceptable.

22. Statistical analysis

Review the qualification of the biostatistical experts involved before and throughout the entire clinical trial procedure, as mentioned in the protocol, commencing with the design of the protocol, randomization, case-report forms (CRFs) and the completion of the final report and/or publication of the results. Review data where possible.

23. Study report

A report reflecting the conduct and outcome of the study should be available after completion of the study. Where possible, the report format should be as recommended in ICH guidelines.

During the inspection, review the report to ensure that the results, data and information presented in the report are a true reflection as obtained in the trial.

Verify that:

- All demographic data, criteria, results, deviations, protocol violations, adverse events are accurately documented in the report;
- The report is signed and dated by responsible persons including the investigator.

24. Multicentre trials

A multicentre trial should normally be conducted simultaneously by several investigators at different sites following the same protocol. During the inspection, review the procedures and administrative arrangements in place to ensure that the study was planned and conducted according the GCP and in accordance with the protocol.

In the review, confirm through verification that there;

- Was written acceptance of the protocol and its annexes by all investigators;
- Were approvals obtained for the protocol and amendments;
- Were records for the meetings between parties involved in the trial;
- Were records (as for single centre trials) for randomization, IMP distribution and storage, training;
- Were standardization of methods for evaluating and analysing laboratory and diagnostic data;
- Was adherence to the protocol, monitors and reports;
- Was a means of centralized data management and analysis;
- Was compliance with procedures e.g. for preparation of the final report;
- Was publication of the trial results;
- Were safety reports provided to investigators from all sites involved in a multicenter trial.

25. Summary

At the end of the inspection, compliance with at least the following should have verified:

- the principles of GxP;
- the Declaration of Helsinki, CIOMS guidelines;
- the protocol;

- the requirements set by the EC;
- the requirements set by the National Regulatory Authority;
- data integrity principles.

At the end of the inspection, at least the following should have been reviewed:

- Master lists for subjects;
- Documentation relating to the Investigational Medicinal Products (IMPs), including COAs, accountability, reconciliation and dispensing records;
- Laboratory results and source data, ECGs and X ray films;
- Logs, registers and records;
- Training procedure and records;
- Lists of staff present during each study;
- Screening records (including general screening forms and data)
- Master list of signatures of volunteers;
- Meal records, (correspondence with dietician and caterer where applicable);
- Custodian reports;
- Sample transfer records
- Adverse Drug Event reports;
- Concomitant medication records;
- Informed Consent Forms;
- Documented justification for the number of volunteers for the study;
- Demographic data recorded versus those reported;
- IMP dispensing records;
- Product administration / dosing records;
- Blood sample collection records;
- Case Report Forms.

References

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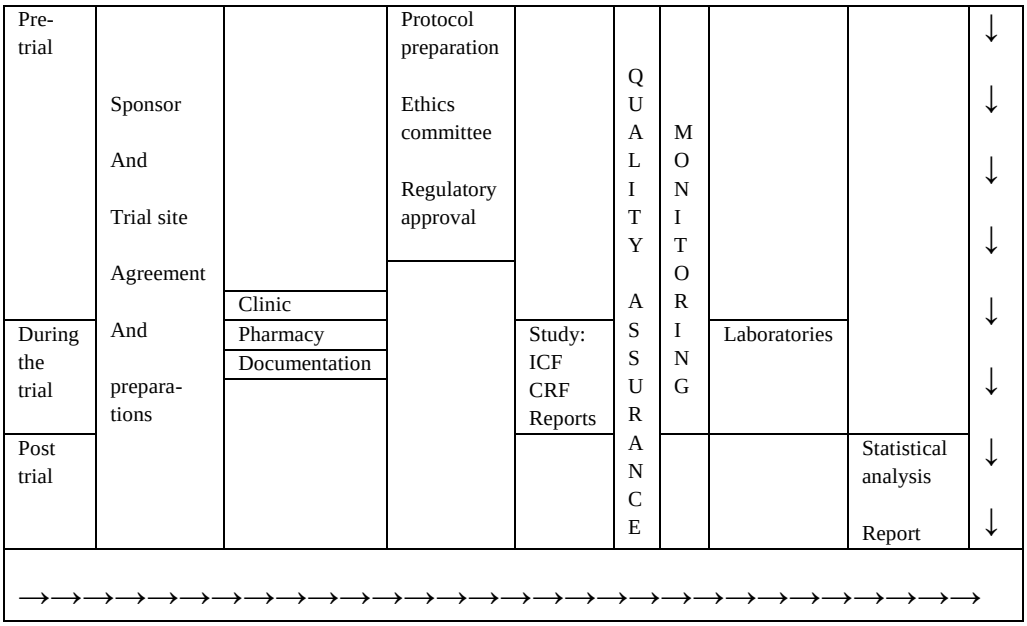
Flow chart



The guide is following steps relating to general stages in preparation of documentation, approvals, and the conduct of a trial. This is an example of the process flow, and not a requirement