Q&A: Good clinical practice (GCP)

Investigational medicinal products (IMPs) in bioavailability and bioequivalence trials

1. How should the packaging of IMP be performed?

(GMP guidelines, §4.18: Before any packaging operation begins, there should be recorded checks that the equipment and work station are clear of previous products, documents or materials not required for the planned packaging operations, and that equipment is clean and suitable for use).

The packaging should be performed in such a way as to limit the risk of possible mix-up between the test and reference product. To this effect:

- the test and the reference product should be packaged during separate operations and should not be available simultaneously in the packaging area;
- during these operations not only should the test and reference products be kept separate, but also all material used for the packaging of each product (containers, labels) and the batch record documents. Material used for different products should not be available in the packaging area simultaneously;
- reconciliation should be performed for the quantities of IMP units, containers and labels introduced in the working area, used during the packaging and remaining after these operations, before the area is cleared and before the packaged IMPs are released;
- the working area should be cleared of all IMP, packaging material and documents between the packaging operations of the test and of the reference product (line clearance). If packaging is performed for several trials successively line clearance should be ensured between each product and each trial;
- once the packaging has been completed for all products to be packaged for a given trial and the products have been released, the packaged test and reference products can be taken simultaneously into the packaging area for further operations (e.g. sorting the containers per subject number);
- critical steps should be controlled in-process by appropriately qualified and trained staff.

In the case of liquid formulations the volume packaged should be measured with appropriate precision and accuracy. If a reconstitution of the product is needed the instructions provided with the product should be followed. If a specified volume of fluid is to be used for the reconstitution this volume should be measured with appropriate precision and accuracy.

At least the following elements should be checked in-process by the operator and independently by a second person:

- line clearance before and after packaging;
- information on the labels, labelling of the containers, compliance with the randomisation code;
- identity of the product introduced in the working area (name, batch number, formulation), consistency with the identity mentioned on the labels, compliance with the protocol, consistency between the physical appearance of the product and the description of the product in the batch release certificate provided by the sponsor;
- for each container, number of IMP units introduced into the container, compliance with the protocol requirements;
- in the case of a liquid formulation: adequate reconstitution of the product if needed, volume
A standard operating procedure (SOP) should describe the packaging operations step by step, including
the controls to be performed at each step and the responsibilities of each person involved.

These operations should only be performed by authorised personnel, qualified by training and education.

Access to IMPs should be limited to authorised personnel, both before and after packaging. Storage
conditions should conform to the provisions of the protocol (temperature, humidity, protection from light
if and as appropriate).

2. How should the packaging be documented?

All operations performed, including the controls, should be documented in detail step by step at the time
each action is taken. The persons performing each task should be clearly identified (operators and
controllers). All precautions taken to avoid mix-ups should be documented in the batch records. Batch
records should include at least the following information:

- line clearance before the start of the packaging operations, and between the packaging of
different products;
- date and time the packaging operation is started and completed, for each product;
- identity of the product packaged, including the batch number, expiry date and a physical
description of the product;
- type of container used for packaging, including the closing/stopping material;
- numbers of the subjects for whom the product is prepared, or precise reference to the
randomisation list followed (reference number, seed used to generate the list). In such a case a
copy of the randomisation list, which should be dated and signed when edited, should be attached
to the batch record;
- number of IMP units dispensed per container;
- if the IMP was provided to the CRO packaged under blister strip, whether the IMP was removed
from the blister or whether the blister was cut and the IMP dispensed while still in a piece of
blister strip;
- in the case of a liquid formulation, how the product was reconstituted if applicable, material used
to measure the volume dispensed/packaged into each container; and expiry date of the finished
product if applicable.
- number of IMP units, containers and labels introduced in the working area, used and remaining
(reconciliation);
- mention of any special problem or unusual events, and signed authorisation for any deviation from
the instructions;
- release of the packaged products after all checks and controls are completed (authorisation to use
the products for the trial after all necessary verifications have been performed and the necessary
documentation has been completed).

Copies of the labels, showing they have been checked against the randomisation list and approved,
should be appended to the batch records.

All controls performed, and the identity of the person(s) performing each control, should be documented
with the signature of the individual in charge.

As the test and reference product are to be packaged separately the use of separate batch records per
product is strongly encouraged. If IMP are to be packaged/dispensed during separate operations for each
trial period, separate batch records should be kept for each period.

3. How should the containers be labelled?

Labelling shall be such as to ensure protection of the subject and traceability, to enable identification of
the product and trial, and to facilitate proper use of IMP.

Labelling of the containers should conform with the local regulatory requirements.

The labelling on each container should comprise at least the following information:
4. How should IMP administration to the subjects be documented?

The use the words "dispensation" or "dispensing" to refer to the provision of a prepared dose of an identified medication to the subject is not recommended in order to avoid possible misunderstandings and confusion. This operation is more properly defined as administration. Administration includes directly introducing the medication into or onto the individual's body.

The process for IMP administration to the subjects should be described in an SOP.

The documentation generated at the time of IMP administration to the subjects should indicate unequivocally the identity of the product administered to each subject, except in the case of a blinded trial. Several possibilities exist to document this administration adequately:

- use of a tear-off label, to be stuck on the case report form (CRF) at the time of IMP administration. This ensures confidence that each subject indeed received the IMP that was packaged for him. An appropriate documentation of the packaging operations is of the utmost importance;
- documentation of the identity of the IMP directly in the CRF at the time of IMP administration. If this information is read directly from the label on the IMP container an appropriate documentation of the packaging operations is of the utmost importance. If there is a physical difference between the test and the reference product (e.g. difference in pharmaceutical formulation, colour, shape, markings) it is recommended to record this physical characteristic in the CRF at the time of administration. The subject might be asked to sign a statement with a description of the IMP he is given, in a language understandable to him. If the documentation on the packaging is insufficient this physical characteristic should be used to check the identity of the product administered against the randomisation list. This check should be documented at the time of administration.

The number of IMP units administered to each subject should be documented at the time of administration.

Compliance with the requirements of the protocol regarding the conditions of administration should be documented: volume of water taken with the IMP, administration in the fed or fasted state, posture etc.

GCP matters

1. Can a sponsor prospectively approve deviations (so-called "protocol waivers") from the inclusion/exclusion criteria of the approved protocol without additional approval of the ethics committee and competent regulatory authority?

Adherence to the protocol is a fundamental part of the conduct of a clinical study. Any significant change to the protocol should be submitted as an amendment to the competent regulatory authority and ethics committee. Significant changes to the protocol include any change in inclusion and exclusion criteria, addition or deletion of tests, dosing, duration of treatment etc (see the definition of a substantial amendment in the 'detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and
declaration of the end of the trial' published by the European Commission in chapter I, volume 10 of the
rules governing medicinal products in the European Community). Deviations from the inclusion/exclusion
criteria of the protocol might erode the scientific and ethical value of the protocol and its authorisation
and might have an impact on the processes put in place for the care and safety of the study subjects.

Sponsors and investigators should not use systems of prospectively approving protocol deviations, in
order to effectively widen the scope of a protocol. Protocol design should be appropriate to the
populations required and if the protocol design is defective, the protocol should be amended.

GCP does permit deviations from the protocol when necessary to eliminate immediate hazards to the
subjects but this should not normally arise in the context of inclusion/exclusion criteria, since the subject
is not yet fully included in the trial at that point in the process GCP inspectors have observed a number of
sponsors implementing systems where the investigator can contact the sponsor, usually the Medical
Monitor, and request a prospective approval to deviate from the inclusion and/or exclusion criteria. The
use of such systematic waiver systems in clinical trials is not considered to be appropriate and studies
using such a system might be regarded as non-compliant with GCP.

2. GCP sets out responsibilities for the sponsor and the investigator, but tasks are increasingly undertaken by a
range of contractors - how should this situation be addressed?

Niche subcontractors are used increasingly for carrying out specific tasks of the sponsor, such as
monitoring, data management, Interactive voice response systems (IVRS), management of electronic
patient diaries or CRFs etc. In addition there are contractors who undertake tasks that are partly or
wholly related to the responsibilities of the investigator, even though the contractor may have their main
contract with, and be paid by, the sponsor (such tasks may include specialised testing, source data
retention (especially in the context of e-CRF or e-patient diary) or patient recruitment or follow-up
contacts).

This fragmented distribution of tasks could put additional strain on the maintenance of quality assurance
and compliance and obscure the clear responsibility and reporting lines for these tasks.

Great care is therefore needed in ensuring that the distribution of tasks is clearly documented and
agreed, that each party has the control and access to data and information that their legal
responsibilities require and that the ethics committees and regulatory authorities approving trials have
been properly informed of these activities as part of the clinical trial application process.

The legal framework:
The responsibility for the conduct of clinical trials is assigned, by Directive 2001/20/EC¹, and by the note
for guidance on GCP (CPMP/ICH/135/95²), to two entities - the sponsor and the investigator.

The roles of the sponsor, investigator, contract research organisation (CRO) and, monitor, are further
defined and described in Directive 2005/28/EC³ and in the glossary and chapters 4 and 5 of the note for
guidance on GCP (CPMP/ICH/135/95).

A number of the tasks involve access to, review, collection and/or analysis of data, much of it personal
data, and in specific cases contact with study subjects or potential study subjects. Data protection
legislation needs to be followed, in addition to the clinical trial legislation and guidance. Directive
95/46/EC⁴ sets out requirements for the protection of individuals with regard to the processing of
personal data and on the free movement of such data. The specific requirements foreseen by local
legislation, setting out the provisions for personal data protection, ethical review and informed consent,
should be followed.

Contracts and agreements

All the clinical trial related tasks are ultimately the responsibility of either the sponsor or the investigator.
Great care should be taken that the relative distribution of tasks to the different parties is well defined,
making clear the ultimate responsibilities in the context of each clinical trial. This should be carefully
documented, in the protocol, procedures, contracts or agreements and other documents.

The specifics of each particular clinical trial need to be taken into account when planning the trials,
during their conduct and monitoring and by audits or inspections.
This is particularly important where entering into novel arrangements that may arise, for instance in the case of site management organisations (SMOs) or other organisations conducting tasks that relate to the responsibilities of the investigator but where the organisation has its contract and funding with the sponsor. These tasks can often involve contact with the study subjects.

The sponsor/CRO should determine the extent of monitoring of each party, within the context of GCP, under particular circumstances. This should be justifiable, and ensure GCP compliance, in the context of the clinical site organisation and the nature of the product and protocol being studied.

**Contact with patients**

Where direct contact with study subjects or their carers/guardians is involved, the privacy and confidentiality of those involved and of any information maintained or collected needs to be respected in compliance with the GCP and clinical trial requirements and with the personal data protection legislation. Such contacts need to be considered in advance by the ethics committees concerned and be given a positive opinion, either as part of the study specific opinion from the ethics committee or a more general opinion in the context of subject screening procedures, which are not study specific.

Personal details such as identity or contact information should not be communicated outside of the parties who have received the ethics committee approval and should not be used or communicated for purposes other than those agreed by the ethics committee and consented to by the study subjects, and where applicable, their carers or others who may be contacted and whose details might be retained.


2. **CPMP/ICH/135/95 note for guidance on GCP**


**3. How are where should source data be defined?**

**Introduction**

Source data is defined in International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) GCP (1.51) as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data should be accurate, legible, contemporaneous, original, attributable, complete and consistent.

Source data is documented in source documents which may be both electronic and on paper. The following list gives examples of source documents where source data may be located:

- medical records
- laboratory reports
- subject diaries
- nurses' notes
- dispensing logs
- electrocardiogram (ECG) print-outs
- case report forms (CRF)
- X-ray images
- radiological reports, etc.
Purpose of identifying source data location

Verification of source data is a considerable part of the work of monitors, auditors and inspectors.

During GCP inspections, it is frequently seen that data are recorded in multiple locations at a site.

It is therefore essential to the possibility of reconstructing the clinical trial that it is clear, where the original record is documented. The identification list of where source data is documented is primarily intended as a tool for monitors, auditors and inspectors in their work of verifying that the trial is performed in keeping with the ICH GCP guidelines, current legislation and guidelines as well as the trial protocol.

Requirements for source data

According to ICH GCP (6.4.9), the protocol should identify any data to be recorded directly into the CRFs that are considered to be source data.

According to the recently published reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials, a detailed diagram and description of the transmission of electronic data should be provided in the protocol. The source data and their respective capture methods should be clearly defined prior to subject recruitment (i.e. in the protocol or in a trial specific source data agreement). The sponsor should describe which data will be transferred, the origin and destination of the data, the parties with access to the transferred data, the timing of the transfer and any actions that may be triggered by real-time review of those data.

It is the expectation of the GCP Inspectors’ Working Group that investigators are aware about the location of the source data and consistent in recording them. The intended location should be clearly defined prior to subject recruitment. One way of achieving this is to generate a source data location list. This list should be prepared by the site and should be signed and dated by the principal investigator or by a person whom the principal investigator has assigned this task. The list should be filed in the investigator's trial master file.

As the location of source data could vary from one investigator site to another, it could be appropriate to make the list site specific.

The list of source data must be sufficiently detailed

In order to facilitate location of data, the list of source data should be sufficiently detailed. It is often not enough to write ‘medical record’, as the medical record is often a collective name covering different document types and locations. This may make it necessary to write: ‘patient record – dispensing and administration chart’, ‘medical record – continuation’, ‘medical record – nurses notes’, etc.

4. How can proper documentation of eligibility be ensured?

It is frequently seen during GCP inspections that the CRF is designed to only include an overall statement regarding a subject's eligibility in the trial. The text in the CRF could for instance say: ‘Did the subject satisfy all study entry criteria?’. The statement is typically intended to be answered with ‘yes’ or ‘no’.

The expectation of the GCP Inspectors’ Working Group is that adherence to all individual inclusion and exclusion criteria are documented in the source data. Adherence to the criteria of the protocol can originate from different sources like blood samples, physical examination, medical history, information from the subject etc. When designing the protocol and the related CRF, the sponsor should carefully consider where each source data originate from, with reference to a specific visit. This is important since some data originate from screening visits, others from the randomisation visit and some data could be historical.

It should be agreed with the investigator of a site how adherence to the individual criteria is documented.

It is the expectation that a qualified physician who is an investigator or a sub-investigator for the trial has assessed each individual eligibility criteria and has taken the final decision to include the subject in the trial (ICH GCP 4.3.1). This decision should be documented prior to the subject receiving the first dose of
GCP inspections have revealed a substantial amount of cases where the overall eligibility statement in the CRF confirms subject eligibility but where source data shows that the subject did not fulfil all eligibility criteria. In addition, it has often not been documented that an investigator/sub-investigator has reviewed all criteria prior to inclusion. It therefore seems that a system with an overall statement in the CRF regarding a subject's eligibility in itself does not ensure the safety of the subjects, the quality of the data and sponsor oversight.

In addition, see related Q&A regarding how and where source data should be defined.

5. What are the expectations of the investigator's copy of the CRF when using a web based application?

Response:

The requirement for investigators to keep a copy of the CRF has been in existence for 20 years. (See for example ICH GCP 8.3.14). It is the expectation of the EU GCP IWG that the copy held by the investigator is a contemporaneous and independent copy of the CRF, i.e. that it is not held or has been held by the sponsor. This requirement is valid irrespective of the media used; however, the introduction of electronic CRFs in clinical trials presents an additional challenge in achieving this requirement - especially if data are being submitted directly via a web based application. This issue has been identified by EU GCP inspectors and discussed in the reflection paper EMA/INS/GCP/454280/2010 (see section 6.2 Specific Requirements Topic 3: control).

Recent inspections have revealed a need to clarify this point.

Requirement 10 of the above reflection paper states the following: "The sponsor should not have exclusive control of a source document. (Requirement 10, ICH GCP 8.3.13)"

The 12 requirements in the reflection paper originate from the CDISC standard and are therefore quoted directly in the reflection paper. However, although the CDISC requirements specifically relate to source data, the requirements is considered by the EU inspectors to be also applicable to transcribed data - as stated in the reflection paper section 6.2. Therefore, the requirement of a contemporaneous and independent copy of the CRF is valid irrespective of whether the CRF contains source data or only transcribed data. The EU GCP inspectors do not consider the requirement above to be met if data are captured in an electronic system and the data are stored on a central server under the sole control of the sponsor. This is because the investigator does not hold a contemporaneous and independent copy of the data.

The EU GCP inspectors do not have a preference for any specific solution e.g. a third party vendor, printed data prior to transferring to the database or saving a contemporaneous copy at the investigator's local computer hard drive; the essential point is that choosing an electronic solution should not jeopardise the credibility of data and should not result in lower quality as compared to a paper CRF. It is the responsibility of the sponsor and the investigator to institute a process by which a contemporaneous and independent copy of the CRF is available at the investigator site.

6. Question: Can the sponsor require that the investigator contacts sponsor staff before unblinding study medication?

Can the sponsor require that the investigator contacts sponsor staff before unblinding?

According to international guidelines, the treating physician (investigator) is responsible for the medical care of the individual trial subject (Declaration of Helsinki 3§ and ICH GCP 4.3). The coding system in blinded trials should include a mechanism that permits rapid unblinding (ICH GCP 5.13.4). If the blinding is prematurely broken, it is the responsibility of the investigator to promptly document and explain any unblinding to the sponsor (ICH GCP 4.7).

The medical care of the trial subjects includes medical decisions such as whether to start or stop treatment or institute alternative treatment if required. In emergency situations the treating physician, often an investigator, may need to break the treatment code immediately, or as quickly as possible if he/she finds it is in the best interest of the trial subject. Consequently, in order to do so, the investigator must have unrestricted and immediate access to break the treatment code.
Some sponsors have recently introduced a code breaking system that requires the investigator to contact a sponsor representative and only after discussion with the representative, the investigator receives information that unblinds the treatment. Some sponsors have even added a requirement that the investigator submits a written form after the phone call before receiving the information that unblinds the treatment.

It is the opinion of the EMA GCP Inspectors Working Group (GCP IWG) and the Clinical Trial Facilitation Group (CTFG) that the responsibility to break the treatment code in emergency situations resides solely with the investigator. Consequently the sponsor can’t require or insist on being involved in the decision to unblind, stall or delay in any way the unblinding of trial subject treatment in emergency situations. The groups also strongly recommend that any sponsor who has introduced or is applying such a system should immediately revise it in order to be compliant with international guidelines.

Breaking the treatment code is usually conducted via code envelopes or electronic systems such as telephone or web based systems such as IVRS and IWRS. When using these kinds of systems the investigator must have direct access in order to break the blind without the interference of the sponsor in any way. In support of electronic systems, a backup system enabling unblinding of treatment must be provided. The CTFG and the GCP IWG acknowledge that such backup systems are operated by the sponsor in a manual way and that the investigator or other treating physician can contact the sponsor staff to unblind the treatment. Still, the sponsor is not entitled to stall or reject unblinding.

Code breaking instructions should be specified clearly in the clinical trial protocol.

Expectations of European Union (EU) competent authorities on the use of electronic trial master files

e-TMFs can be acceptable to regulatory authorities if they meet the requirements for TMFs that are described in Directive 2005/28/EC and the related guidance in volume 10 of the rules governing medicinal products in the European Union. For the purposes of GCP inspection (and audit), the following attributes apply:

- The e-TMF should allow review in an efficient manner, analogous to that possible with paper TMFs. Such a review should not take longer to access than for a paper TMF. (Efficient, straightforward navigation and opening of documents permitting searching and browsing (analogous to leafing through a paper file).
- Inspectors/auditors should have direct access to the e-TMF and the documents held in the e-TMF (the live system, not a copy) to allow direct searching.
- Documents held on an e-TMF should be evidently authentic, complete and legible copies of the original documents.
- The e-TMF system should have validated methods for preventing any changes being made to the TMF documents, this includes the process of transferring from original media to the electronic medium.
- The process for transferring original TMF documents to e-TMF (or other media) should be robust and have been validated to prevent failure of transfer the entire content of the original TMF without loss (i.e. there should be a demonstrable 1:1 mapping between the content of the original TMF and the e-TMF).

Additional considerations

Documents on e-TMF should remain complete and legible in all aspects giving information about the way the document was prepared. This holds especially for contracts and forms completed by hand. Transfer to e-TMF should not (be used to) conceal any physical change to the document such as physical cut & paste to remove or add items, use of correction fluid etc.
It is helpful if the e-TMF has:

- A folder structure to allow easy identification of TMF sections.
- A folder/file naming convention that readily identifies what each file/document is, so inspectors/auditors do not have to open numerous documents to locate those they need.
- The ability to open more than one document at a time to allow comparison (so size of screens or double screens important).
- The ability to provide access to the same type of document across all studies/sponsors/product etc (i.e. if inspector needs to review documents for all/some selected studies/sites).

**Future considerations**

For the future, it would help if e-TMFs were available through secure internet links. This would help to avoid some unnecessary travel when accessing the TMF. This approach has advantages over supplying e-TMFs by e-mail, DVD etc., in that only one version of the e-TMF needs to exist, which can be continually updated for ongoing trials.

**Advantages**

- Assisting the development of virtual inspections.
- Improving the efficiency of the inspection process (and lowering the carbon footprint of trial management, inspection and audit).

**Records of study subject data relating to clinical trials**

1. **What are the roles and requirements for the study subject record (medical record) and related source documents in the context of a clinical trial?**

**Background**

A variety of records is generated and maintained relating to the healthcare of clinical trial subjects (whether study subjects or healthy subjects). Some of these are general and relate to the general healthcare of the study subject before, during and after the trial. Others are specific to the trial. A clinical trial as a scientific undertaking requires careful record-keeping to ensure that data are collected and reported in an accurate and complete manner. In addition regulations and guidelines have established processes including investigator review, monitoring, auditing and inspection, in order to check and control the accuracy and completeness of the data. GCP, ethical requirements and medical standards require that each study subject is cared for and this duty to the individual is put above the more general scientific needs.

There are national, professional, local, or institutional requirements either in law, various forms of guidance, rules, or established practice which define many requirements for the maintenance of records in the course of normal study subject care. Any requirements that may arise as a consequence of the conduct of clinical trials can only be an addition and not a substitute for these, since the conduct of a clinical trial should never diminish the standard of care.

Many of those involved in clinical research ask questions about what should be documented, when, where, by whom and for what reason.

The purpose of this document is to set out some of the main elements of this study subject record-keeping in the clinical trial context, in order to assist those involved in clinical research to understand why such records are kept and looked for, and in order to help in planning record-keeping in specific contexts.

Taking into account the various issues outlined it is very unlikely that a CRF would ever suffice as the complete and only record of a study subject relevant to their participation in a clinical trial.

Reference documents: [Note for guidance on GCP (CPMP/ICH/135/95)](#)
Specific references

Study subject care - CPMP/ICH-GCP 2.3, 2.7, 4.3
Source Data /documents - CPMP/ICH-GCP 1.51, 1.52, 5.15, 8
Original Medical Record - CPMP/ICH-GCP 1.43
Case Report Form - CPMP/ICH-GCP 1.11, 6.4.9, 4.9, 8

Issues

What should appear in the original medical record?

- The medical record is a key element of study subject care. It ensures that an ongoing record of information relating to the study subject, visit records, test records, medical history, diagnoses, treatments etc. are available to the treating physician and his or her colleagues or peers who may intervene in the care of the study subject or take over that care. As such it has a role before, during and after the clinical trial per se.
- Any information that would routinely be expected to appear in a medical record should continue to appear there during the study to ensure the care of the study subject is maintained.
- The fact that the study subject is in a clinical trial, its identity and any specific information over and above the routine that impact on the study subject care should also appear, or be clearly referenced and readily available to the care giver.
- The medical record may also be the first place in which trial related data is recorded and as such becomes by definition the source document for that data.
- It may also be the main point of information on medical history for the purposes of the study, even if that information was originally recorded elsewhere.
- The medical record should provide sufficient baseline information to permit the investigator to enrol the study subject in the trial with due recognition of the needs of medical care and in compliance with the protocol.
- The medical record is also the common point of confirmation of study subject identity and demographics.

What purposes does the medical record serve in the context of the clinical study?

- Study subject care
- Source document
- Corroborating/supporting document – the medical record is generally a document with some legal status, open to degrees of peer review, and completed in many cases by several people. As such it serves as an important supporting document to corroborate data reported to the sponsor in the CRF.
- For example identity and patient existence, demographics, medical history, diagnosis, participation in the clinical trial, IMP and concomitant medication, intercurrent illness and adverse events. In addition, various protocol related measurements may appear here or in related documents (laboratory reports, ECGs, X-rays and reports etc).
- Where the protocol has described that certain data may be recorded solely in the CRF - this in general is taken to mean multiple repeat measurements, rating scales, study subject diaries.

What purpose do source documents serve?

- Prompt and accurate recording of study data.
- A source from which the CRF can be completed.
- Quality control and other verification and corroboration (monitoring, audit, inspection) of study data and study conduct/protocol/GCP compliance.

What characteristics should source data documents have?

Source documents should be:

- Accurate
- Legible
- Contemporaneous
- Original
- Attributable
- Enduring
- Available and accessible