

GUIDELINES FOR RETENTION OF CLINICAL TRIAL RECORDS AT INVESTIGATOR STUDY SITES

INTRODUCTION

During the conduct of a clinical trial, large quantities of documentation are generated both by the sponsor of the trial and by the investigator. These documents permit evaluation of the conduct of the study, the quality of the data produced and serve to demonstrate the compliance of the investigator, sponsor and trial monitor with the standards of Good Clinical Practice (GCP) and with all applicable regulatory requirements.

It is essential that documentation at the sponsor and investigator sites is filed correctly and in a timely manner to assist in the management of the trial and to assure auditors and inspectors that the trial has been conducted in accordance with all relevant regulations.

This guideline has been issued:

- to assist clinical trial investigators in the management of clinical trial documentation;
- to be used by sponsors to assess the suitability of new investigator sites during the pre-study evaluation process; and
- to provide guidance to sponsors during study monitoring.

DEFINITIONS

Documentation: all records in any form (including hard-copy documents and documents stored electronically on magnetic or optical media) describing the methods and conduct of the trial, factors affecting the trial and the actions taken.

Investigator: one or more persons responsible for the practical performance of a trial and for the integrity, health and welfare of the subjects during the trial.

Investigator file: documentation held by the investigator relating to a clinical trial including, but not limited to, the protocol, informed consent documents, subject codes, case report forms (CRFs), ethics committee approval and general correspondence.

Patient file: a file or files containing the demographic and medical information about a patient or a subject (e.g. a hospital file or a consultation record). Such files are necessary for the verification of the authenticity of the information presented in the CRF and, where needed, the possibility of completing or correcting it.

Sponsor: an individual or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial. An investigator, hospital or academic institution may assume the role of sponsor if they independently initiate and take full

responsibility for the trial.

INFORMATION

Before participating in a clinical trial, potential investigators should be made fully aware of the requirements placed on them. Applicable regulations identify some of the responsibilities of the investigator related to trial records and documents. These include:

- to ensure that he/she has sufficient time to conduct and complete the trial and has adequate staff and appropriate facilities which are available for the duration of the trial
- to manage code procedures and documentation with meticulous care
- to collect, record and report data properly
- to make all data available to the sponsor/monitor and/or relevant authority (where required) for verification/audit/inspection purposes
- to ensure that the confidentiality of all information about the subjects is respected by all persons involved as well as the information supplied by the sponsor

Directive 2001/83/EEC states:

- the investigator shall arrange for the retention of the patient identification codes for at least 15 years after the completion or discontinuation of the trial. Patient files and other source data shall be kept for the maximum period of time permitted by the hospital, institution or private practice.

It is clear therefore that before embarking on a clinical trial both the potential investigator and sponsor must assess the facilities and staff available to ensure that they are able to meet the requirements for clinical trial records management to the satisfaction of the sponsor and regulatory authorities for the requisite period of time. The sponsor should identify to the potential investigator the documents which will need to be retained and the retention times for this documentation, making reference to relevant guidelines. The retention schedule, including any actions to be taken prior to document destruction, should be agreed **before** commencement of a study.

The facilities required to enable the investigator to fulfil their obligation are not explicitly stated, being described only as "appropriate". The following guidelines are therefore an interpretation of the phrase "appropriate facilities" based on the experiences of regulatory inspections and current practices by records management professionals and may be used as the basis for a checklist by the investigator or study monitor (see appendix). The standards described are those that are reasonably expected to be achieved by the majority of investigational sites. In many cases, the guidelines describe the minimum standards (see paragraphs enclosed in a box); it is expected that where resources allow, these standards would normally be exceeded. An appendix has been provided which can be used as an aide-mémoire by either the

investigator or study monitor.

1. Confidentiality

Filing space should be available for the storage of investigator files during the conduct of the clinical trial. Investigator files will normally be stored in an investigator's office or local filing area initially and subsequently transferred to a central filing area or off-site commercial storage facility.

The investigator must ensure that the confidentiality of all information concerning patients and information supplied by the sponsor is respected by all persons involved and at all times in accordance with accepted ethical practices and any confidentiality agreements with the sponsor.

Investigator files must be clearly marked to identify the sponsor and the clinical trial number. To reduce the likelihood of documentation from one sponsor being misfiled with that from another sponsor the use of clear, distinctive file markings is recommended; for example, different coloured files or different coloured file index inserts for different sponsors. Where study monitors are granted access to files relating to their studies, care should be taken that documentation pertaining to other studies cannot be viewed. It is normal practice for the investigator to sign a statement of confidentiality with the study sponsor. This may be a legally binding agreement in which case non-compliance could result in legal proceedings being taken against the investigator by the sponsor.

2. Environmental conditions

The minimum requirement is for documentation to be stored in conditions that minimise the risk of damage or loss of information. The risk of damage from water should be reduced by storing documentation above floor level and away from overhead water pipes. Documentation should be located in areas with minimal variation in temperature and humidity if stored for long periods of time.

The environmental conditions under which documentation is stored become increasingly important during longer-term storage. The ideal environmental conditions are a stable, ambient temperature of between 13°C - 18°C and relative humidity between 55% - 65%. Dust levels should be kept to a minimum.

Trial records may also include data recorded on media other than paper e.g. microfilm, floppy disks, compact disks, computer tapes, x-ray film. Where possible the environmental conditions should be appropriate for the particular type of record being stored:

- Magnetic media e.g. tapes and disks
 - Temperature range 18°C - 20°C and relative humidity 35% - 45%;

- Film e.g. photographic, x-ray
 - Temperature range 10°C - 18°C and relative humidity 35% - 45%

If these conditions cannot be met, the following ranges are broadly acceptable:

- temperature 13°C - 16°C, relative humidity 50% - 60%.

However, a stable environment is as important as having the temperature and relative humidity within the above range.

3. Security

Investigators or the hospital/institution must ensure that data are recorded and stored properly and have not been tampered with. Access to documentation should therefore be restricted to authorised personnel only. For central filing areas, this can be achieved by controlling access and/or assigning responsibility for the maintenance and control of files to a named individual(s). It is recommended that filing rooms are fitted with intruder alarms to detect unauthorised access. Where appropriate, the investigator should liaise with relevant personnel to encourage the provision of such facilities.

The minimum requirement is for investigator files to be stored either in lockable cabinets or in a lockable room. When not in use and when unattended, the cabinets or room in which investigator files are located should be locked to assure the confidentiality and security of information contained therein.

Where data are stored electronically e.g. on a personal computer, precautions should be taken to control access to the data as recommended in the EU guidelines on Use of Computerised Systems in GxP Environments. Consideration should be given to retaining a duplicate data tape in a fire-proof safe or in off-site storage.

Where records are being transferred between locations (for example from an investigator's office to central storage or from central storage to off-site storage), precautions should be taken to ensure the integrity, security and safety of the data at all times. Records should be appropriately labelled and, where necessary placed in sealed containers.

Fire precautions are normally the subject of national legislation, local by-laws and building regulations.

The minimum requirement is for either (i) an automatic fire detection and extinguishing system or (ii) fire-detection and the provision of readily accessible fire-fighting equipment. Smoking in document storage areas must be strictly forbidden.

Fire precautions for central filing areas should be more stringent than those for other areas

having a similar level of risk because of their irreplaceable contents and potential commercial and/or research value. Documentation should be stored in a room fitted with an automatic fire detection and alarm system and preferably in fire-retardant cabinets. Portable fire-fighting equipment should be readily available in or near to document storage areas. Water is not advisable as the primary fire extinguishing system due to the damage that it can cause to documentation but is preferable to no extinguishing system at all. Dry powder, carbon dioxide or a halon-substitute extinguisher should be used, if possible. The use of automatic, non-aqueous fire extinguishing systems should be considered.

4. Record keeping

Investigators must ensure that data are recorded and stored correctly and accurately. This not only includes data recorded on documentation returned to the sponsor (e.g. case report forms) but also original source data (e.g. patient files), laboratory data and pharmacy data (e.g. drug dispensing and drug accountability records).

Such files should be kept up-to-date and should be maintained in an orderly manner. Similarly, any indices, registers or databases which identify the location of clinical trial data must be well maintained. Any systems used should be independent of the individuals running the clinical trial such that when investigator personnel leave the employment of the establishment, relevant trial data can easily be located by succeeding staff.

Where the investigator is unable to ensure adequate storage of data on site for the period of time specified in Directive 2001/83/EC or according to additional requirements specified by the sponsor, the sponsor may supply the necessary resources to assist with adequate retention e.g. digitisation or alternative physical storage facilities. However, the investigator, hospital or institution must retain control of the data at all times and any change of custodianship must be documented. Measures must also be adopted to ensure the confidentiality of the data at all times and that procedures for the retention of such data is agreed and documented with the institution. Where data is transferred to off-site storage facilities the sponsor must assure himself that they are satisfactory for this purpose and that data may be made available if requested by relevant authorities.

CONCLUSION

Good record-keeping both during the conduct of a clinical trial and for the period following the trial can reflect the high standard of work achieved by the investigator. It is frequently crucial to the success of the trial and to compliance of the sponsor and the investigator with GCP. The discussion of records storage facilities and procedures should therefore be made a key aspect of the pre-study visit by the sponsor and during subsequent site monitoring visits. The investigator should recognise the importance and benefits of good records management practices and take appropriate measures to comply with the requirements of the sponsor and with GCP.

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REFERENCES

- 1 The Rules Governing Medicinal Products in the European Community, Vol. III, (Addendum), July 1990: Guidelines for Good Clinical Practice.
- 2 91/507/EC Commission Directive of 19 July 1991 modifying the Annex to Council Directive 75/318/EEC on the approximation of the laws of Member States relating to analytical, pharmacotoxicological and clinical standards and protocols in respect of the testing of medicinal products.
- 3 Good Clinical Trial Practice - Nordic Guidelines
- 4 International Conference on Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use (ICH) Draft Tripartite Text - Good Clinical Practice: Addendum on Essential Documents. Released for consultation at Step 2 of the ICH Process 27 October 1993.
- 5 BS5454:1989 British Standard Recommendations for the Storage and Exhibition of Archival Documents.
- 6 EFGCP Update Paper: Good Clinical Practice and Computer Use at Investigator Sites.

APPENDIX MANAGEMENT OF CLINICAL TRIAL RECORDS AND THEIR RETENTION

<ul style="list-style-type: none"> • Is adequate space available for short-term storage of trial records? Do you know how much space is needed? 	<ul style="list-style-type: none"> • Is adequate space available for long-term storage of trial records? Do you know how much space is needed?
<ul style="list-style-type: none"> • Are trial records from different sponsors adequately differentiated? 	<ul style="list-style-type: none"> • Can specific clinical trial records be easily identified and retrieved?
<ul style="list-style-type: none"> • Are environmental conditions for records storage acceptable? 	<ul style="list-style-type: none"> • Are there sufficient staff to maintain quality record keeping systems?
<ul style="list-style-type: none"> • Are trial records free from risk from fire, flood, theft or vermin? 	<ul style="list-style-type: none"> • Is security of records storage acceptable?
<ul style="list-style-type: none"> • Is access to trial records controlled? 	<ul style="list-style-type: none"> • Are there procedures for the relocation of data in the event of an emergency e.g. closure of facility?
<ul style="list-style-type: none"> • Do records storage areas have adequate fire protection? 	<ul style="list-style-type: none"> • Are procedures in place to identify the location of trial records following the departure of the investigator?
<ul style="list-style-type: none"> • Are current records, including laboratory and pharmacy records, adequately maintained? 	<ul style="list-style-type: none"> • Are investigator/hospital computerised systems in compliance with GCP regulations (access controlled; validated; documented procedures)?
<ul style="list-style-type: none"> • Are records management policies and procedures acceptable and applied? 	<ul style="list-style-type: none"> • Are remote data entry systems in compliance with GCP regulations?