Risiken erkennen – Gesundheit schützen

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Notice of a consensus document of the National and Länder Working Party on Good Laboratory Practice on the archiving and storage of records and materials

of 5 May 1998

The Principles of Good Laboratory Practice were brought into German chemicals legislation by the Chemicals Act (ChemG) in the version promulgated on 25 July 1994 (Federal Law Gazette p. 1703).
This consensus document sets out in detail the requirements for the archiving and storage of records and materials in accordance with Annex 1 Nos 10.1 and 10.2 of the Chemicals Act. It replaces the version promulgated on 14 October 1993 (Federal Gazette p. 10077).

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pp.
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Content

Consensus document of the National and Länder Working Party on Good Laboratory Practice (GLP) on the requirements for the archiving and storage of records and materials in accordance with Annex 1 Nos 10.1 and 10.2 of the Chemicals Act in the version promulgated on 25 July 1994 (Federal Law Gazette p. 1703).

I. Archiving and storage of records

1. Scope

Special attention should be paid to the following relevant provisions, guidelines and instructions:

- Doc 440 by the *Arbeitsgemeinschaft für wirtschaftliche Verwaltung e.V.* (Working Group on Economic Administration) entitled “Legal requirements of storage procedures and storage media ", 1989
- DIN 19070
- Annex to the letter from the Federal Minister for Finance of 1 February 1984 - IV A 7 - S 0318 - 1/84 - "*Grundsätze für die Mikroverfilmung von gesetzlich aufbewahrungspflichtigem Schriftgut*" (Basic principles for the microfilming of legally-stored records)

2. Definitions and explanatory notes

The following provides clarification of the Principles of Good Laboratory Practice in accordance with Annex 1 of the ChemG.

2.1 Study plan

The study plan is a document which describes the whole scope of the study.

Explanatory note:

The approved study plan is generally a written document. A study plan based on a GLP-compliant LIMS (Laboratory Information Management System) satisfies these requirements

when access authorisation and approval procedures exist and are set down in standard operating procedures.

When the study has been completed, the study plan can be archived on paper, microfilm, computer file or optical disc.

2.2 Raw data

Raw data means all original laboratory records and documentation, or verified copies thereof, which are the result of the original observations or activities in a study.

Explanatory note:

The key characteristics of raw data are:

- they must be legible or visibly recognisable/presentable;
- they must be necessary and appropriate for reconstructing a study.

Raw data can appear on paper as handwritten records or printed versions, as photographs, films, video prints, graphs or computer files on data media (e.g. magnetic, optical).

GLP principles permit the use of verified copies in the place of originals (e.g. including scaled-down technical copies). This may be necessary in duly justified cases, e.g. the poor storage stability of the media carrying the raw data (such as thermo print paper). A documentary record must be kept of the checks carried out on such copies to verify that they are complete and correctly reproduce the original raw data.

Paper documents must be dated and initialled, and computer files must be subject to appropriate control procedures in compliance with access rights.

The procedure must be described.

2.3 Specimens

Specimen means any material derived from a test system for examination, analysis, or retention.

Explanatory note:

The rules mentioned under point II.2 only relate to those specimens which have been derived from biological systems.

2.4 Samples

Sample means a quantity of the test or reference item.

2.5 Test item

The test item is a chemical substance or mixture which is tested. A test item can also be a material of biological origin, a micro-organism or a virus, or a component of micro-organisms or viruses.

Explanatory note:

This also includes biologically produced test items such as prepared formulations.

2.6 Reference item

The reference item (control substance) means any well designated chemical substance or mixture other than the test item, which is used to provide a basis for comparison with the test item.

2.7 Calibration substance

The GLP principles give no definition for "calibration substance".

Explanatory note:

The calibration substance is a chemical substance used to:

- check the functioning of physical and chemical test systems;
- adjust physical and chemical test systems.

Calibration substances should be treated as reagents in the sense of Annex 1, Section II of the ChemG.

2.8 Final report

The GLP principles give no definition for "final report".

Explanatory note:

The final report is a written document which must meet the requirements of Annex 1, Section II, No 9 of the ChemG. Several original copies of a final report can be drawn up and signed and dated at the same time, in which case they must be identical and individually identifiable (e.g. Number 1 of 3 original copies).

2.9 Other documents

The GLP principles give no definition for "other documents".

Explanatory note:

The term "other documents" covers all records kept in accordance with GLP requirements (Annex 1 Section II No 10.2 para1 b, c, d, e of the ChemG), as well as other documents such as floor plans, organisation charts and operating instructions, but only insofar as they are referred to in the study plan and standard operating procedures.

This category can also include documents relating to the tests, such as telephone messages, delivery notes etc.

Documents which are accessible to the general public do not need to be archived.

2.10 Archive

The GLP principles give no definition for "archive".

Explanatory note:

An archive is a locked room or a separated and locked area in a room (e.g. a cupboard), in which GLP records and materials which need to be archived are kept in good order and safety. An archive can be housed in several rooms or buildings with different equipment.

Access authorisation must be given.

2.11 Archive manager

The GLP principles give no definition for "archive manager".

Explanatory note:

The archive manager is a person who is designated by the management of the test facility to be in charge of the archives. Depending on the size of the facility, other persons can also be designated and specific tasks delegated to them. These persons – and the archive manager as well - can carry out other activities too, but may not be a study director or be involved in the study.

In justified exceptional cases (e.g. in small test facilities) a member of the quality assurance unit can be the person in charge of the archives.

3. Requirements of an archive

Archives must be designed and equipped for the housing and secure storage of documents and materials. The management of the test facility should ensure this by taking appropriate measures which are to be described in a standard operating procedure. It is the task of the archive manager to ensure that these measures are carried out.

The study director is responsible for transferring all documents and materials to the archive.

Inventories should be compiled of the archived documents. Archived material is to be indexed to ensure that they are stored in orderly fashion and can be retrieved quickly.

Indexing is carried out in accordance with the test facility’s requirements and can, for example, be done using lists, card file systems or computer programs.

Access to the archives is limited to persons authorised by the management. Records are to be kept of all documents and materials borrowed and returned.

Measures must be taken to prevent all the possible events listed below, whereby a combination of a number of the measures listed may be appropriate:

3.1 Subsequent modification or loss of documents and materials

The possible countermeasures are:
- to keep inventories of documents and materials
- to regulate access *
- to account for all documents and materials borrowed and returned
- to control the issue of original documents as regards
  - the numbering or pagination of the documents against the table of contents
  - the bindings of the documents
- to use microfilm or other processes such as optical disk records
- to hand over copies of original documents only
- to allow original documents or materials to be consulted only under supervision in the archives.

* N.B:

It is not necessary to keep a visitor's book.

3.2 Prevention of loss of, or damage to, documents or materials due to fire

The possible countermeasures are:
- No smoking or open flame
- Use of fire-resisting equipment depending on the fire risk
- Installation of warning devices (smoke detectors)
- Provision of appropriate fire-extinguishing equipment (gas or dry-powder extinguishers), give directions to the fire service responsible.

N.B:

The use of water to extinguish smaller fires should be avoided.

3.3 Prevention of loss of, or damage to, documents or materials due to adverse environmental conditions

Adverse environmental conditions may include:

3.3.1 *Condensation*

One possible countermeasure is:

- to ventilate or heat the room sufficiently.

3.3.2 *Damp*

Possible countermeasures are:

- insulation of water pipes
- floor drainage
- water detectors.

3.3.3 *Pests*

Possible countermeasures are:

- appropriate hygiene measures
- pest control (if necessary).

3.3.4 *High temperatures*

It is generally assumed that temperatures up to 40ºC present no risks for paper (the exception being thermo papers for which the countermeasure is to copy onto normal paper). For samples and specimens, as well as certain data media (microfilms, magnetic media) it can be necessary to regulate the temperature.

3.4 Loss due to theft

Possible countermeasures are:

- keep the archive locked
- regulate access
- burglar alarm (if necessary)
- store copies in a separate place.

4. Documents on microfilm

Microfilming is to be carried out in accordance with the “Basic principles for the microfilming of legally-stored records" and AWV document 440.

Once original documents have been filmed and it has been confirmed that they have been transferred correctly, they must be stored until the next inspection by the authorities, or for at least 3 years.

Documents which are filmed more than 3 years after they have been archived can be destroyed once it has been confirmed that they have been transferred correctly.

When the authorities carry out an inspection, the documents filmed must be presented on request in paper form (re-enlargement).

Documents are not to be microfilmed if their condition is such that problems may arise in filming them or if re-enlargement might no longer permit full and reliable analysis.

For the long-term archiving of microfilms, the temperature should be below 21ºC and the relative humidity between 15% and 50% (DIN 19070).

5. Documents in electronic form

Documents in electronic form are to be kept in accordance with the aforementioned requirements for the safety of archive material (Point I.3) and AWV document 440 Section II 4. Attention should also be paid to the following:

5.1 Room climate

The temperature and relative humidity for the storage of electronic documents must lie within the limit values indicated by the manufacturer.

If no such indications are available, the temperature should be between 15ºC and 25ºC and the relative humidity 30-60%.

5.2 Magnetic fields

There should be no electrical machinery/appliances with strong magnetic fields in the vicinity of archives for magnetic media (tapes and disks). The recommendations issued by the manufacturers of appliances with strong magnetic fields regarding the minimum distance to data collection and storage systems must be observed.
If these are not available, a safe distance of 0.5 to 1 metre should be observed from sources of strong magnetic alternating fields such as motors, generators and electric cables carrying strong currents.

5.3 Dust

The data media are to be protected from the effects of dust, e.g. by using dust-proof packaging (original packaging) and keeping them away from major sources of dust. Optical disks are to be stored in closed cartridges and protected from light and dust.

5.4 Storage and data security

The magnetic media (tapes, cassettes, diskettes) are to be stored standing side-by-side (and not piled on top of each other), in order to minimise physical pressure on them.

As a preventive measure to avoid data loss, it is recommended that the data are copied either every two years or as stipulated by the manufacturer of the data medium. As a method of protection against external influences such as fire or water, a back-up copy can be made and kept separate from the original copy.

The identity of back-up copies must be guaranteed by appropriate measures and documented. Point I 2.2 applies accordingly.

5.5 Data media conversion

If, as a result of the rapid development of hardware and/or software, it becomes necessary to convert the data media, validated software should be used for this purpose. The software and version used must be documented.

When transferring electronic data to the archive medium, it is recommended that the output format chosen is appropriate to ensure the independence of specific analysis software or database structures.

Software for the reconstruction of results from the raw data is to be kept for as long as it is possible to use it on the hardware, but for no longer than the period for which the accompanying data are stored.

6. Documents on optical disks

The procedures to be used for optical storage media are similar to those for microfilms and electronic documents.

7. Archive contracting facilities

A) Officially supervised and recognised GLP archive contracting facilities are authorised to assume responsibility for the secure storage of archive material over a given period of time. The relevant details are to be set out in a contract with the test facility responsible for carrying out the study. Aside from this, in accordance with GLP principles, the test facility responsible retains the ultimate overall responsibility for carrying out the study beyond compilation of the final report up to the point of archiving the original documents and materials. The basic GLP principles state that this body must indicate where these materials are archived in the final reports. It must be guaranteed in the contract that the archive material can be presented without delay upon the request of inspectors during an inspection visit for the purposes of the study audit in the test facility responsible.

An application should be made to the appropriate supervisory authorities by the management of the archive contracting facility for GLP inspections to be carried out. All documents (including contracts) and materials must be made available for inspection at any time in accordance with the ChemVwV-GLP (Administrative Regulation concerning chemicals - Good Laboratory Practice).

B) A precondition for an archive contracting facility is compliance with all the relevant requirements of the GLP Principles and consensus documents.

C) The following points should be implemented by an archive contracting facility and regulated, where appropriate, by standard operating procedures (SOPs):

a) Presentation of the legal form of the archive contracting facility.
b) Definition of the archive contracting facility management.
c) Documentation of the responsibilities of personnel.
d) GLP training for personnel.
e) Internal and/or external quality assurance.
f) Secure and appropriate premises (break-in, fire, water, etc.).
g) Rules for access restrictions, authorised persons, supervision.
h) Rules for inspections by the test facility responsible or the supervisory authority.
i) Handling of the archive material as a complete package:
   The test facility responsible collects the archive material, which is packed, closed and/or sealed as appropriate, and provides information on the storage conditions or any hazards relating to the storage of substances or other materials.
   The archive contracting facility takes charge of the archive material, checks – as far as possible – and documents to what extent the archive material is complete, transports it, if necessary, to the archive, and indexes and stores it in unmistakable fashion (taking into account confidentiality, security, etc.)
j) Prevention of subsequent modification, damage or loss of archive material during storage.
k) Rules on handing over archive material at the request of the authorities, e.g. for upcoming inspections of the responsible test facility or for dealing with queries by

the authorities (the test facility responsible must ensure and confirm that the material returned is complete and unmodified).

l) Consultation of the archive material by the test facility responsible only under the supervision of the archive contracting facility (e.g. to copy individual documents).
m) Documentation of all procedures (storage, issue, consultation etc.).
n) Procedures regarding the cessation of activities by the archive contracting facility (e.g. notifying the test facility in advance and returning the archive material to the test facility responsible or its legal successor).
o) Consultation with the supervisory authority in the case of the cessation of activities by a test facility without a legal successor regarding the further handling / disposal of documents and materials.

II. Duration of storage of samples and specimens

1. Storage of samples

The sample (reference sample) is used to subsequently check the identity of a test item. The quantity of samples and storage conditions is to be determined in accordance with this purpose.

The provisions in force relating to radioactive substances must be observed.

Samples must be stored at least until the next inspection by the authorities, at any rate for two years from the date of the quality assurance audit of the final report, but for no longer than fifteen years.

Excluded from the minimum duration of storage are those samples which decompose during the storage period or could constitute a threat to storekeeping. These samples are to be stored for as long as they do not constitute such a threat.

This is to be documented and notified in advance to the quality assurance unit.

2. Storage of specimens

The storage of specimens should facilitate the task of checking results.

a) Specimens which have undergone such physical and/or chemical changes during a study that further results cannot be obtained, do not need to be stored. This also includes any residues obtained from specimens which have been studied.

b) The examples given below of minimum periods of storage from the date of the quality assurance audit of the final report apply to specimens obtained as the result of a study:

Test system	Type of sample	Analysis	Minimum duration of storage
Various toxicological tests	Cryostat sections	Histopathology	2 years
	Formalin or alcohol-fixed specimens (wet material)	Histopathology	5 years
	Paraffin blocks	Histopathology	12 years
	Paraffin sections	Histopathology	12 years
	Blocks	Electron microscopy	12 years
	Slides	Electron microscopy	12 years
	Slides	Histochemistry	12 years
	Electropherograms Cellulose acetate films	Protein determination	5 years
	Marrow smears	Cell morphology	12 years
	Blood smears	Differential blood count	5 years
	Blood smears	Reticulocyte count, Heinz bodies	2 years
Embryo toxicity tests	Alizarin stained foetal material	Foetal morphology	12 years

Test system	Type of sample	Analysis	Minimum duration of storage
In vitro mutagenicity tests			
Chromosomal aberrations, DNA repair, Sister Chromatid Exchange	Slides	Chromosome morphology, autoradiography	12 years
In vivo mutagenicity tests			
Chromosomal aberrations, DNA repair, micronucleus test, SCE-Test	Slides	Chromosome morphology, autoradiography, cell morphology	12 years

c) All other specimens apart from those listed above must be stored at least until the end of the quality assurance audit of the final report. The quality assurance unit must be notified in advance of the end of storage in all cases.