“Good Laboratory Practice”

What is behind all this?

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Summary

The effects of the thalidomide scandal are still felt, which is why the next generation will probably also be aware of it. And the victims not only have to contend with the actual impact of the scandal, but also with its later effects such as increased joint degeneration due to malposition.
“Good Laboratory Practice” (GLP) should prevent such a scandal from happening again, which is why it has been introduced worldwide. As a quality assurance system, it encompasses all organizational structures and the sequence of analyses and tests for authorization of a medicinal product. Especially important with GLP are protections against manipulation of the raw data as manipulation would promote or accelerate approval. In this way, effort could be made to ensure that the time and costs for the “non-clinical” studies were not in vain.
For this reason, GLP not only regulates the personnel, space and equipment-specific requirements, but also the responsibilities during and after testing. And so the four eyes principle applies. Therefore, several signatures are also required for the approval documents.
Only upon approval is a scientific evaluation carried out, which is why it is necessary to submit all documents in their entirety. If documents are incomplete, approval is delayed or not granted as missing documentation from analyses or testing are deemed nonexistence at this point. Therefore, it is particularly important to submit all documents in their entirety to ensure approval.

Content

Introduction to “Good Laboratory Practice”

The “Good Laboratory Practice” regulatory mandate (GLP) was introduced in 1978 after the FDA (U.S. Food and Drug Administration) had already identified significant deficiencies in toxicological studies in the years preceding. All means were taken to ensure that the long development time and costs for a drug approved for the market were not in vain. Perhaps the best known example of errors in toxicological studies was the thalidomide scandal, the extent of which today is still not entirely clear. Therefore, the impact of abnormal biomechanical stress on other joints and supporting elements for those injured cannot be assessed.

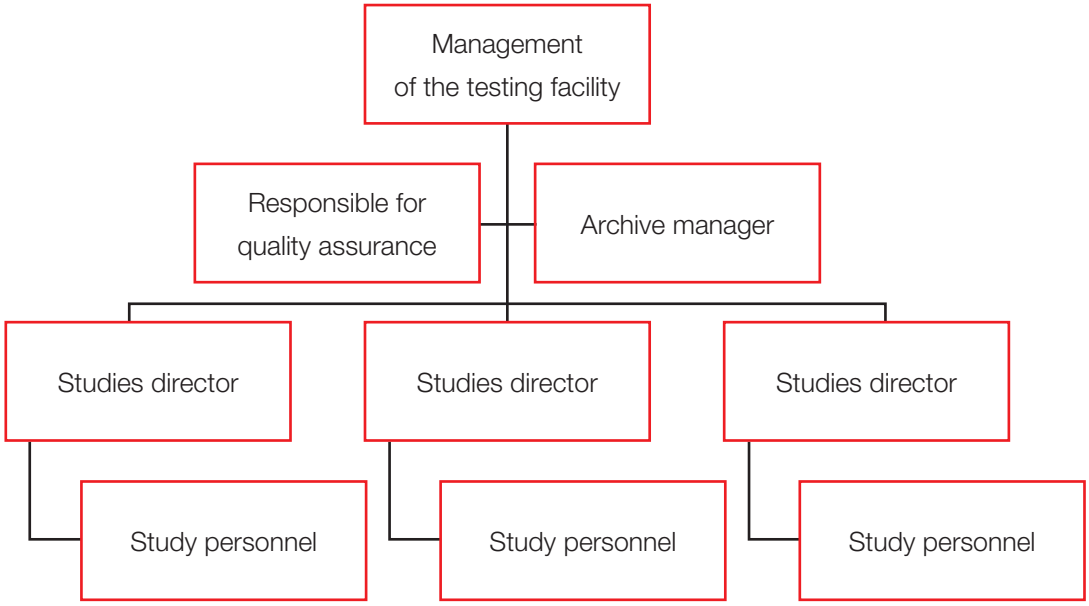
For this reason, a quality assurance system had to be created that deals with the organizational procedures and framework conditions of non-clinical safety tests. Non-clinical testing includes all laboratory studies not conducted on humans. In addition, only certain substances are subject to GLP, the so-called “regulated” substances. These include drugs, pesticides and chemicals. Especially in drug development, ecotoxicological studies, toxicological and safety pharmacology testing must be carried out in accordance with GLP principles. It can be said in summary that in general, GLP is to be applied as soon as documentation for approval must be created.

GLP was introduced worldwide to ensure the reliability of data and of course, the international recognition of data. In particular, value is placed on accountability, traceability, assignment of responsibilities and safekeeping. A scientific evaluation is only carried out upon approval.

Accordingly, GLP regulates personnel and space requirements, as well as other organizational requirements such as the infrastructure of the test facility and the subject of planning and implementation of GLP testing.

Organization
Organization of human resources

For the organization of a GLP, certain human resource requirements are necessary to ensure safekeeping and compliance. The organization of human resources is independent of the company or institutional hierarchy.
An establishment like a testing facility that wants to test according to GLP must be staffed as following.



The management of the testing facility carries the (entire) responsibility for the organization and function of the test facility and for the budget. The management is also responsible for compliance with GLP principles in the testing facility.
The studies director assumes management of the respective GLP testing and responsibility for compliance of the testing with GLP principles. These include in particular implementation and reporting.
The study personnel are also responsible for the quality and reliability of the data. Particular attention should be paid to properly recording the raw data, which should be carried out promptly and accurately.

Organization
Organization of human resources

For those responsible for archiving and quality assurance, it is important to note that they are not permitted to participate in the GLP testing itself to ensure a certain degree of independence. External companies can also take over these tasks.
This represents a significant increase in human resource costs, which leads to problems for smaller institutions in staffing all positions. In addition, rules for representation must be made, so that additional staff is needed. To support smaller institutions, it is possible as assign multiple responsibilities to one person. Ultimately, there are staffing costs for just 2 people if archiving responsibilities and quality assurance are handed over to a third party. These two people are responsible for management of the testing facility and the studies director.
But where is a “personnel union” possible?

	Testing facility management	Studies director/ test personnel	Archive manager	Quality assurance
Testing facility management		Not possible	In exceptional cases	Not possible
Studies director/ test personnel	Not possible		Not possible	Not possible
Archive manager	In exceptional cases	Not possible		Yes limited
Quality assurance	Not possible	Not possible	Yes limited	

In addition, certain personal details must be saved such as the professional career, job description and regular training with certificates. These documents are to be regularly updated and kept up to date.

Organization
Premises and equipment

However, not only are there high demands on personnel, but also specific requirements for the facilities and equipment. GLP areas must be identified and be separate from other areas. This separation begins with the storage of supplies of laboratory animals to husbandry to the laboratories themselves.

Certain requirements are also placed on the equipment used and on computer-supported systems in particular. It must be assured at all times that such systems are functioning properly, which can be confirmed by regular inspection, cleaning, maintenance and calibration.

Logbooks must also be maintained for the equipment used for GLP in order to track its use and functional tests. In addition, operating instructions as well as maintenance and repair documentation must be available.

Computer-supported systems also have to be developed, validated, operated and maintained in accordance with GLP principles. Furthermore, there must be an access policy in place, be it through physical or logical access protection (password protected). Another international standard, the GAMP 5 guidelines, has to be complied with in regards to validation in particular.

Especially in the area of computer-supported systems, testing facilities can save significantly by purchasing GLP-compliant equipment. BINDER GmbH offers special software for its simulation chambers that already meets GLP requirements, thus making the entire simulation chamber compliant. The workload is thus reduced for the testing facility and the simulation chamber can be used straight away for GLP testing.

Furthermore, specific requirements are placed on archiving such as strict access control that only allows access to the archive manager and his/her representative. However, another person may enter the archive when accompanied. This strict rule should prevent manipulation of the documents. Currently, the retention period is at least 15 years, so that the size of the archive must be chosen based on the number of GLP tests.

Organization
Testing and reference items

When working in the laboratories, it is crucial that all reagents are properly labeled with reference to shelf life and opening date. In addition, the usual safety and hazard symbols must be also attached.
If the shelf life is exceeded, the test object must be disposed of. Alternatively, an expert can extend the expiration date if properly documented on the object with comment. Such an extension can be made based on an analysis, which must also be thoroughly documented.

Operating procedures

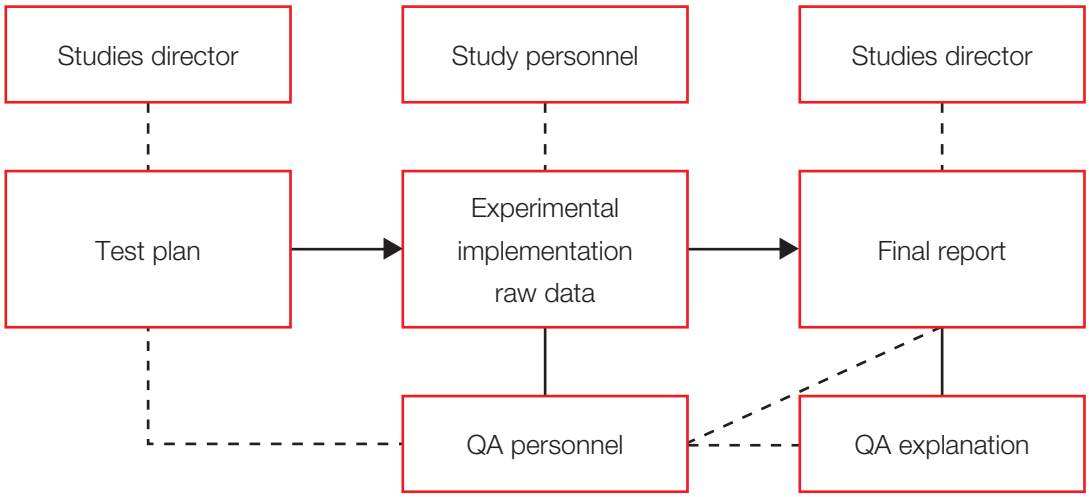
Standard operating procedures are used for GLP that must be available at each work station. These procedures describe general activities that are relevant to GLP. Each testing facility creates its own operating procedures, which must be regularly reviewed and updated.
Requirements determined according to GLP are placed on such standard operating procedures. For this reason, an operating procedure must be available in written form at every work station in its current version only. With regards to content, such a procedure must describe and define the GLP-related activities.
The operating procedures must be written specifically for each testing facility and be treated as confidential. Templates are available for use, but they must be adapted accordingly and approved by management of the testing facility. A standard operating procedure is thereby binding for testing personnel.
These procedures must cover at least 8 areas and cause no delays in approval.

- Testing and reference items
- Equipment, materials and reagents
- Record keeping, reporting, storage and retrieval
- (Biological) test systems
- Quality assurance procedures
- Procedures for test/analysis methods
- Computer-supported systems
- “Interfaces” with internal and external institutions if necessary

After creating a standard operating procedure, it must be signed by the author and reviewer. It must then be released by Quality Assurance and then approved by the director of the testing facility. Only after these four signatures are found on the document it can be distributed.

GLP testing sequence

In preparation for GLP testing, a study director must first be appointed who then creates a test plan. The test plan must be available before the study specific experimental work is started and be approved by the director of the testing facility, Quality Assurance and the ordering party. Only then can testing begin.



The test plan includes a chronological description of the test procedure, as well as the test methods and frequency of execution. This information is binding after approval of the test plan and may only be amended in urgent cases. Any change must be documented accordingly in a supplement to the test plan. A distinction is made here in

- Changes to the test plan necessary with amendments, modifications, updates or corrections of information

and

- Test plan deviations required due to unforeseen events, accidents or human error.

GLP testing sequence

GLP testing is carried out based on the test plan and documented accordingly. In the documentation, care must be taken that it is complete, intuitive and accurate and can be assigned at any time to the test. In addition, all data must be signed with the testers initials and date. In this way, the traceability of the data should be ensured throughout the testing and thereafter. There can also be Quality Assurance inspections that monitor compliance with GLP principles.
If GLP testing has been completed, it is finished with the final report. An abridged report must be created for even aborted tests. The report must be created by the study director and then released by Quality Assurance, who adds an explanation and inspection results.

Approval

Approval is granted once all documents are completed, documented and archived. Only then a scientific evaluation is carried out. On approval, anything not documented has not been performed. Missing documents can cause a product to not be approved and can lead to the loss of years of work, time and costs.
This system of quality assurance should serve to prevent any hasty approvals in which not all eventualities are covered. A standard is set with GLP that makes manipulation impossible and standardizes the approval procedure regardless of where the drug was developed.

Imprint

Author

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Company profile

BINDER is the largest specialty manufacturer of simulation chambers for science and industry in the world. With its technical solutions, the company contributes significantly to improving the health and safety of people. Our range of products is suitable for routine applications, highly specialized work in research and development, production and quality assurance. BINDER GmbH is located in the South of Germany and employees 350 people worldwide

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Sources

Course materials for the introduction of “Good Laboratory Practices” QL334-18 of the Center for Advanced Technological and Environmental Training in Karlsruhe, Germany, part of the KIT