Implementation of the OECD principles of good laboratory practice in test facilities complying with a quality system accredited to the ISO/IEC 17025 standard

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Summary. Laboratories with a quality system accredited to the ISO/IEC 17025 standard have a definite advantage, compared to non-accredited laboratories, when preparing their facilities for the implementation of the principles of good laboratory practice (GLP) of the Organisation for Economic Co-operation and Development (OECD). Accredited laboratories have an established quality system covering the administrative and technical issues specified in the standard. The similarities and differences between the ISO/IEC 17025 standard and the OECD principles of GLP are compared and discussed.

Key words: good laboratory practice, ISO/IEC 17025 standard, quality systems.

Riassunto *(Adozione dei principi di buona pratica di laboratorio dell'OCSE in centri di saggio conformi al sistema di qualità accreditato secondo la norma ISO/IEC 17025)* Laboratori con un sistema di qualità accreditato secondo la norma ISO/IEC 17025 sono caratterizzati da un significativo vantaggio, in confronto ai laboratori non accreditati, quando predispongono le proprie strutture per l'adozione dei principi di buona pratica di laboratorio (BPL) dell'Organizzazione per la Cooperazionee lo sviluppo Economico (OCSE). I laboratori accreditati posseggono un sistema di qualità documentato che copre tutti gli aspetti amministrativi e tecnici specificati nella norma. Le somiglianze e le differenze esistenti tra la norma ISO/IEC 17025 ed i principi di BPL dell'OCSE sono confrontate e discusse.

Parole chiave: buona pratica di laboratorio, norma ISO/IEC 17025, sistemi di qualità.

INTRODUCTION

The main differences between a laboratory accredited according to the ISO/IEC 17025 standard and a research facility working according to the principles of good laboratory practice (GLP) of the Organisation for Economic Co-operation and Development (OECD) are the types of projects that the laboratories deal with [1, 2]. The GLP principles of the OECD are defined as studies. They are usually long-term, pre-determined experiments for regulatory purposes agreed upon by the sponsor before commencing the work. On the other hand, the accredited tests are generally short-term, employing specific and different analytical methods requested upon submission of samples by the customer for the determination of a given property. Both facilities perform chemical, analytical and microbiological tests. Therefore, a GLP-compliant laboratory wishing to obtain accreditation or, *vice versa*, an accredited laboratory applying for recognition of compliance with the GLP principles, may exploit the available quality system with the addition of the necessary requirements.

This paper presents a short review of the quality system in place for a laboratory accredited according to the ISO/IEC 17025 standard and for a GLP-compliant test facility (TF) as well as of their overlapping aspects. The advantages of an accredited laboratory when preparing for GLP recognition and the additional GLP requirements for such a laboratory are also discussed. Comprehensive tables summarize similarities and differences between the requirements of the two quality systems.

ACCREDITED LABORATORIES

Accredited laboratories working according to the ISO/IEC 17025 standard (updated in 2005) include medical laboratories, building construction and engineering laboratories, pesticide residue laboratories, and laboratories conducting pure material analysis and tests for monitoring, *e.g.*, the environment.

GLP TEST FACILITIES

Non-clinical studies include supporting tests for:
- research in developing a new drug or active material;
- certifying a new pesticide;
- compliance of a new medical device, new equipment and the like;
- monitoring air pollution, etc.;

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Table 1 | *A comparison of the management and technical requirement of the ISO/IEC 17025 standard and the OECD principles of GLP*

Section of the ISO/IEC 17025 Standard	Subject	Accredited laboratory	GLP-compliant TF
4.1	Organization and management	The laboratory should define the duties of: - the technical management - the quality manager for all the activities of the laboratory	For each study there is a need for a: - defined SD - defined quality manager - defined archivist
4.2	Quality system	Quality manual addressing each section of the ISO/IEC 17025 standard	Well-defined quality assurance programme including timetable for QAU checks
4.3	Document control	Establish and maintain procedures to control all documents that are part of its quality system and are unequivocally identified and approved	Documented master schedule for all the studies. Study plans, with relevant documented SOPs and reports
4.4	Review of requests, tenders and contracts	Necessary for tests and calibrations	Not required by the GLP principles
4.5	Subcontracting of tests and calibration	Requirements defined in the Standard	Not required
4.6	Control of services and supplies	Requirements defined in the standard	Not required by GLP
4.7	Service to the client	Requirements defined in the standard	Interaction with the sponsor, prior to commencing the study – Signing the study protocol.
4.8	Complaints	Requirements defined in the standard	Not applicable
4.9	Control of non-conforming testing and/or calibration work	On-going quality control	Part of the QAU programme are on-going checks reviewed regularly and internal audits.
4.10	Corrective action	Requirements defined in the standard	Defined as amendments to the study
4.11	Preventive action	Requirements defined in the standard	Not required
4.12	Control of records	Original observations (raw data), amending records and computer filing	Ensure the maintenance of a historical file of all the procedures
5.1	General	Factors which contribute to the uncertainty, correctness and reliability of the test results	Uncertainty values are not required
5.2	Personnel	Requirements defined in the standard	Current training, knowledgeable in the principles of GLP
5.3	Accommodation and environmental conditions	Sufficient to facilitate the correct performance of the tests	Avoid cross contamination Extr emphasis for studies which involve animals
5.4	Test calibration methods and method validation	Requirements defined in the standard	All methods have to be validated prior to use
5.5	Equipment	Requirements defined in the standard	Apparatus used in a study should be periodically inspected according to the procedures
5.6	Meas Measurement traceability	Requirements defined in the standard	Information concerning source preparations data stability should be available
5.7	Sampling	Requirements defined in the standard	No sub-sampling
5.8	Handling of the test and calibration specimen	Requirements defined in the standard	Chain of custody, test of stability throughout the study, effects of storage conditions, etc.
5.9	Assuring the quality of the test and calibration results	Required in the standard. Participation in PT schemes	On-going predetermined and ad hoc quality checks of the test item, study, and facility. No PT required

GLP: good laboratory practice; SD: study director; QAU: quality assurance unit; SOP: standard operating procedures; PT: proficiency testing.

The GLP principles are usually prescriptive regarding the activities that need to be performed before, after, and during a study. These GLP tests are planned and documented in a detailed protocol. During the experiments periodic monitoring of the documents, the tests, the facility and the overall study is carried out in accordance to the applicable standard operating procedures (SOPs).

SIMILARITIES AND DIFFERENCES

As regards management and organization, issues that are addressed in both the ISO/IEC 17025 standard and the GLP principles include, among others: definition of responsibilities, SOPs for maintenance, calibration, and use of equipment, procedures for the chain of custody (reception, registration and storage of test items/samples), training of staff, retention of valid reference materials, use of valid test methods and test report/study reports.

Areas unique to the GLP principles are as follows: animal care, monitoring of facility and processes including the specific study, availability of the study plans and master schedules for all the studies, and archive.

Areas unique to the ISO/IEC 17025 standard include: processing of complaints, estimation of the uncertainty, service to the client, preventive actions and participation in interlaboratory comparisons such as proficiency testing, traceability and uncertainty of the measurements, and customer review.

A comprehensive comparison of the management and technical requirements of the ISO/IEC 17025 standard and of the GLP principles of the OECD is set forth in *Table 1*.

ADVANTAGES OF AN ACCREDITED LABORATORY

A testing laboratory accredited according to the ISO/IEC 17025 standard has an advantage when preparing for compliance to the principles of GLP since the quality system in place and the technical evaluation of the different tests under accreditation have been assessed. There is controlled documented quality system equipment with the appropriate maintenance, calibration and operating instructions, reference materials, ongoing quality control tests and trained personnel. Not less important is the mentality of the staff and management and that they are at ease with one quality system and have appreciated the ensuing benefits. Therefore, a laboratory wishing to expand its activities to include pre-clinical studies need only to fulfill the additional requirements for compliance with the GLP principles.

ADDITIONAL REQUIREMENTS OF THE ISO/IEC 17025 STANDARD FOR OECD GLP RECOGNITION

Table 2 describes the additional aspects of the GLP quality system not included in detail in the ISO/IEC 17025 standard. In particular, as regards the organizational requirements, according to the principles of GLP, the study director (SD), quality manager and archivist are the three persons who need to be formally appointed and who are each individually responsible for the correct discharge of their duties in compliance with the said principles.

The GLP principles have specific guidelines for the each of these functions (SD, quality manager and archivist) where the responsibilities are defined. These can be summarized as follows:

a) the SD is the only focal point of control for a study. He/she is responsible for the performance of the study in compliance with the principles of GLP, the interpretation of the results and the preparations of the final report. The SD approves the study plan and any amendments. He/she ensures the technical validity and availability of the appropriate procedures and is in constant contact with the quality assurance unit (QAU);

Table 2 | *Requirements specific only to the OECD principles of GLP*

Subject	Accredited laboratory	GLP-compliant TF
Reagents and solutions	Defined in Section 5.6.3.2. Where possible measurement results should be traceable to SI units or to certified reference materials	Certified, fully traceable, with appropriate documentation from the customer or supplier regarding the expiry date, storage, stability and homogeneity, and purity. The analyst should also record these details in the study when used. All reference substances in the GLP context need to be registered in reception and usage uniquely identified as a reference or working standard.
Control of changes	Defined in Section 4.3.3. The laboratory should define how changes are made in documents	Planned amendments to the study protocol should be documented and signed by the SD. Non-planned deviations should be archived with the study.
Animal-related laboratory work, forms a major part of the GLP activities	No reference	Emphasized in detail
Archive facilities	As requested by the customer	Archive facilities should be provided for the secure storage and retrieval of study plan, raw data, final reports, sample of test items and specimens. An archivist should be nominated for this activity.

GLP: good laboratory practice; TF: test facility; SD: study director.

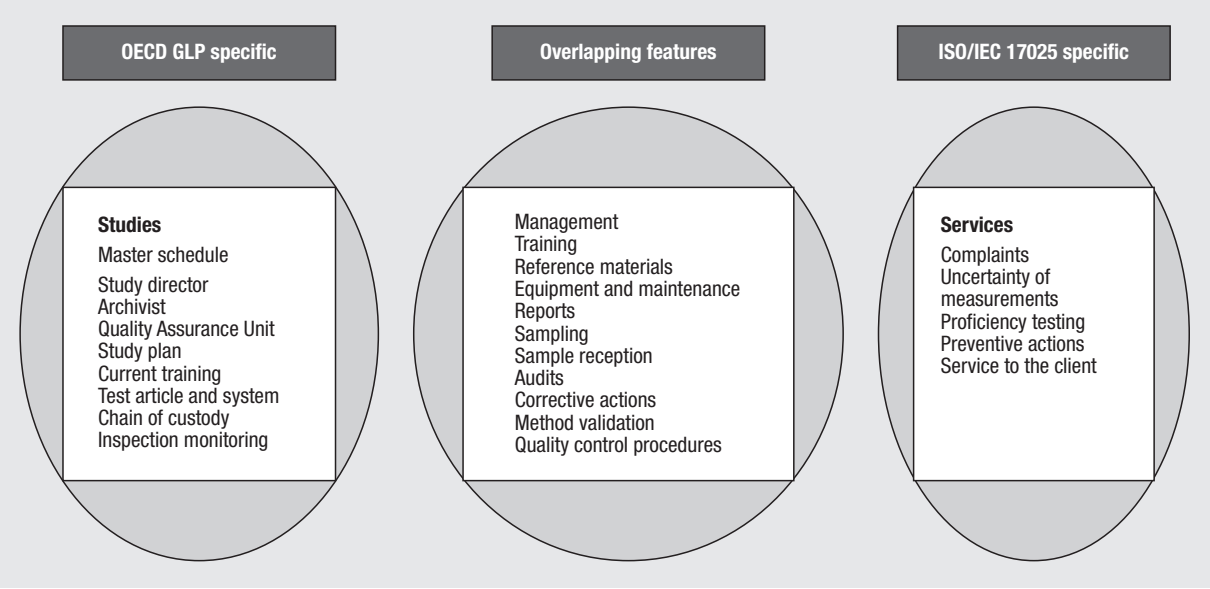

Fig. 1 | *A schematic view of the similarities and differences between the ISO/IEC 17025 standard and the OECD principles of GLP.*

b) the functions of the quality manager are defined in the ISO/IEC 17025 standard (clause 4.1.5 i), although it is only required *that he/she ensures that the quality system is implemented and followed at all times* with direct access to the highest level of management. On the other hand, the QAU in the OECD GLP context has five major duties, *i.e.*: inspecting the study while it is being carried out; auditing the records and documentation, recommending corrective actions and monitoring the follow-up . He/she periodically writes status reports on the study, highlighting problems and the corrective action taken. The quality assurance functions are mandatorily independent of the study;

c) as regards the archivist, the ISO/IEC 17025 standard requires that records are to be kept (clause 4.12) and should be retrievable, though no strict rules are defined as it is the case with the OECD principles of GLP. These principles require that an archivist be designated and that the appropriate resources be available for proper functioning of the archive.

CONCLUSIONS

To summarize, there are similarities in the two quality systems that may complement each other. Much more than this, on the other hand, there are some specific key issues in both the ISO/IEC 17025 standard and the OECD principles of GLP that need to be individually addressed. *Figure 1* sets forth the specific aspects of the two quality systems.

It can be estimated that a laboratory accredited on the basis of the ISO/IEC 17025 standard and wishing to expand its activities to the GLP arena has already complied with approximately 70% of the administrative and technical issues prescribed by the principles of GLP, while the remaining 30% can be set up as an extension of the quality system in place. Last, but not least, depending on the national GLP monitoring authority, it may be not necessary to manage the two quality systems independently from each other, but they could be integrated into one overall system taking advantage of the aspects common to both, provided that there is no impairment of the distinctive features of each of them.

Disclaimer

This manuscript does not necessarily reflect the views of the Author's Company.

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