

REVIEW OF QUALITY ASSURANCE SYSTEM IN ECOTOXICOLOGY LABORATORY

Carmen Mincea

*correspondence address:

Research - Development Institute for Plant Protection

Bd. Ion Ionescu de la Brad nr.8, CP 013813, S1

Bucharest, ROMANIA

Tel.: 004-021-269 32 34

Fax.: 004-021-269 32 39

e-mail: minceacarmen@yahoo.com

Abstract: Laboratories with a quality system accredited to ISO/IEC 17025 have a definite advantage, compared to non-accredited laboratories, when preparing their facilities for the Organization for Economic Cooperation and Development good laboratory practice (OECD GLP) recognition. Accredited laboratories have an established quality system covering the administrative and technical issues specified in the standard. These issues include: internal audits, job descriptions and responsibilities, procedures for equipment/instrument maintenance and calibration, document control, handling of reagents, chemicals and reference materials, sample reception and sampling, validation of test methods, traceability and uncertainty of the tests results, training of personnel, client complaints, corrective and preventive actions. Several of these issues are also required for OECD GLP recognition either with a different emphasis and/or with additional requirements.

Key words: quality system, accredited laboratory, good laboratory

INTRODUCTION

The main differences between an accredited laboratory according to ISO/IEC 17025 and a research facility working according to the Organization for Economic Cooperation and Development good laboratory practice (OECD/GLP) series of principles are the types of projects that the laboratories deal with. OECD GLP projects are defined as studies. They are usually long-term pre-determined experiments agreed upon by the sponsor before commencing the work whereas the accredited tests are generally short term, employing specific and different analytical methods requested upon submission by the customer, with unknown samples.

Both facilities perform chemical analytical and microbiological tests. Therefore an OECD GLP recognized laboratory wishing to obtain accreditation or, vice versa, an accredited laboratory applying for OECD GLP recognition, may use the available quality system with additional necessary requirements. This is similar to the conclusions of Hermbeck in his article on "*GLP and other quality assurance systems*", which showed a general comparison between good manufacturing practice (GMP), good GCP, GLP and accreditation systems.

Making a rough estimate, there is probably about a 70% overlap of the requirements for ISO/IEC 17025 and OECD GLP. The aim of this article is to highlight the similarities between the ISO/IEC 17025 and OECD GLP directives as well as to identify the additional requirements.

This paper presents a short review of the quality system of an accredited laboratory, a GLP testing facility and their overlapping issues. The advantages of an accredited laboratory when preparing for GLP recognition and the additional GLP requirements for such laboratories is also shown. In addition, a comprehensive tabulated comparison according to the management and technical requirements of IEC/ISO 17025 is given in comparison to the requirements of the OECD GLP.

The term "quality" has a relative meaning. This is expressed by the ISO definition: "*The totality of features and characteristics of a product or service that bear on its ability to satisfy stated or implied*

needs". In simpler words, one can say that a product has good quality when it "*complies with the requirements specified by the client*".

In principle, three levels of organization of these laboratory activities can be distinguished. From the top down these levels are:

1. Quality Management (QM)
2. Quality Assurance (QA)
3. Quality Control (QC)

Quality Management

Quality Management is the assembly and management of all activities aimed at the production of quality by organizations of various kinds. In the present case this implies the introduction and proper running of a "Quality System" in laboratories. A statement of objectives and policy to produce quality should be made for the organization or department concerned (by the institute's directorate). This statement also identifies the internal organization and responsibilities for the effective operation of the Quality System.

Note. An even wider concept of quality management is presently coming into vogue: "Total Quality Management" (TQM). This concept includes additional aspects such as leadership style, ethics of the work, social aspects, relation to society, etc. For an introduction to TQM the reader is referred to Parkany (1995).

Quality Assurance

Proper Quality Management implies consequent implementation of the next level: *Quality Assurance*. The ISO definition reads: "*the assembly of all planned and systematic actions necessary to provide adequate confidence that a product, process, or service will satisfy given quality requirements.*" The result of these actions aimed at the production of quality, should ideally be checked by someone independent of the work: the Quality Assurance Officer. If no QA officer is available, then usually the Head of Laboratory performs this job as part of his quality management task. In case of special projects, customers may require special quality assurance measures or a Quality Plan.

Quality Control

A major part of the quality assurance is the *Quality Control* defined by ISO as "*the operational techniques and activities that are used to satisfy quality requirements.*" An important part of the quality control is the *Quality Assessment*: the system of activities to verify if the quality control activities are effective, in other words: an evaluation of the products themselves.

Quality control is primarily aimed at the *prevention* of errors. Yet, despite all efforts, it remains inevitable that errors are made. Therefore, the control system should have checks to *detect* them. When errors or mistakes are suspected or discovered it is essential that the "Five Ws" are trailed:

- what error was made?
- where was it made?
- when was it made?
- who made it?
- why was it made?

Only when all these questions are answered, proper action can be taken to correct the error and prevent the same mistake being repeated.

The techniques and activities involved in Quality Control can be divided into 4 levels of operation:

1. *First-line control*: Instrument performance check.
2. *Second-line control*: Check of calibration or standardization.
3. *Third-line control*: Batch control (control sample, identity check).

4. *Fourth-line control*: Overall check (external checks: reference samples, interlaboratory exchange programmes).

It will be clear that producing quality in the laboratory is a major enterprise requiring a continuous human effort and input of money. The rule-of-fist is that 10-20% of the total costs of analysis should be spent on quality control. Therefore, for quality work at least four conditions should be fulfilled:

- means are available (adequate personnel and facilities)
- efficient use of time and means (costs aspect)
- expertise is available (answering questions; aftercare)
- upholding and improving level of output (continuity)

In quality work, management aspects and technical aspects are inherently cobbled together and for a clear insight and proper functioning of the laboratory these aspects have to be broken down into their components.

ISO 17025 is an International Standard (published by the International Organization for Standardization) that specifies the general requirements for laboratories for the competence to carry out tests and/or calibrations. ISO 17025:2005 was modified to include all of the management requirements of ISO 9001, including document control. (www.itp.gob.pe/ISO/ISO 17025 Laborator.)

ISO/IEC 17025 is the global quality standard for testing and calibration laboratories. It is the basis for accreditation from an accreditation body. The current release was published in 2005. There are two main clauses in ISO/IEC 17025 – Management Requirements and Technical Requirements. (www.ISO 17025.com)

Management requirements are related to the operation and effectiveness of the quality management system within the laboratory, and this clause has similar requirements to ISO 9001.

Technical requirements address the competence of staff; testing methodology; equipment and quality; and reporting of test and calibration results.

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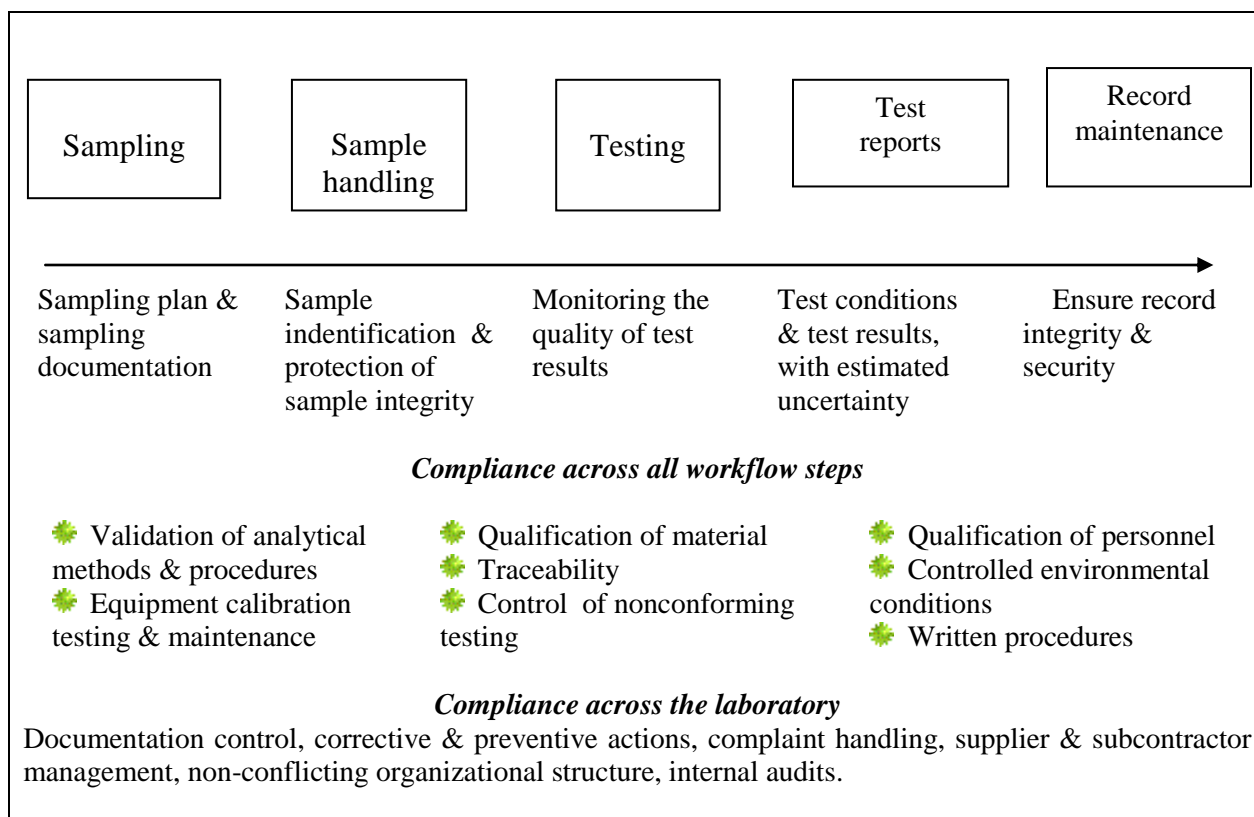
Implementing ISO/IEC 17025 as part of laboratory quality initiatives provides both laboratory and business benefits such as:

- Having access to more contracts for testing and/or calibration. Some public and private organizations only give contracts to accredited laboratories. Accreditation will also help to get more contracts from organizations that don't mandate accreditation, but do give preference to accredited laboratories in competitive situations.
- Improved national and global reputation and image of the laboratory.
- Continually improving data quality and laboratory effectiveness.
- Having a basis for most other quality systems related to laboratories, such as Good Manufacturing Practices and Good Laboratory Practices.

Analytical testing laboratories seeking ISO/IEC 17025 will be impacted in multiple areas. The main difference between good analytical practices and formal accreditation is the amount of documentation to be developed. There is no doubt that any good analytical laboratory uses qualified analysts, checks the performance of equipment used for testing, and validates analytical methods. However, many times the outcome of the tests is not fully documented.

ISO/IEC 17025 accreditation requires formal documented environment–, „what is not documented is a rumor” and is viewed by assessors as „not being done”.

The overall impact of accreditation on an analytical laboratory can be best illustrated by looking at the whole sample/data workflow. Figure below shows a typical laboratory workflow of samples and test data, together with ISO/IEC 17025 requirements.



Laboratory accreditation is an acknowledgement of the laboratory's competences to perform certain actions, by the certifying agency. Accreditation is given upon application of laboratories, after their evaluation and confirmation that they meet the specified requirements and conditions. The basis for meeting the requirements by the laboratory is the PN-EN ISO/IEC 17025:2001 standard "General requirements regarding the competences of research and calibrating laboratories." (www.wikipedia.En.org/wiki/ISO/IEC_17025)

Compliance of laboratory's operations with the requirements of the international PN-EN ISO/IEC 17025:2001 standard certifies about its competences. The requirements included in the standard, which regard the laboratory's management and the technical requirements, regard each laboratory, regardless of its type, size or structure and adopted methods. Meeting the requirements regarding the laboratory's management is equal to meeting the quality management system's requirements included in the ISO 9001 standard, but is not sufficient to confirm the laboratory's competences to perform specific tests or calibrations.

Thus, the second group of requirements of the PN-EN ISO/IEC 17025:2001 standard is related with the laboratory's technical competences and concerns: the laboratory's equipment, measurement consistency, the methods of testing and calibrating as well as their validation, personnel, premises and environmental conditions of taking samples, handling of the testing and calibration objects; ensuring the quality of results and presenting the results.

Confirming the competences to perform certain tests through accreditation, conducted according to world-wide adopted criteria is to ensure that the results are reliable, unbiased and credible and that they can be recognized not only at the state level, but also at the international level.

The company laboratory, which wishes to achieve reliability, credibility and precision of results should adopt the rules of the **Good Laboratory Practice (GLP)**. Good Laboratory Practice specifies the requirements for laboratories regarding personnel, equipments, testing and recording methods. General GLP requirements - Good Laboratory Practice for a testing laboratory cover: Properly trained personnel, standard analytical methods, schedule of frequency of taking test samples, the way samples are taken, proper equipment (controlled and calibrated at a regular basis), storage of the tests' results and system of recordings. (www.tqmc.pl/iso_17025_and_glp.)

Good Laboratory Practice (GLP) embodies a set of principles that provides a framework within which laboratory studies are planned, performed, monitored, recorded, reported and archived. These studies are undertaken to generate data by which the hazards and risks to users, consumers and third parties, including the environment, can be assessed for pharmaceuticals (only preclinical studies), agrochemicals, cosmetics, food additives, feed additives and contaminants, novel foods, biocides, detergents etc.... GLP helps assure regulatory authorities that the data submitted are a true reflection of the results obtained during the study and can therefore be relied upon when making risk/safety assessments. (www.fao.org/docrep).

GLP is a policy for all aspects of the laboratory which influence the quality of the analytical work. When properly applied, GLP should then:

- allow better laboratory management (including quality management)
- improve efficiency (thus reducing costs)
- minimize errors
- allow quality control (including tracking of errors and their cause)
- stimulate and motivate all personnel
- improve safety
- improve communication possibilities, both internally and externally.

The result of GLP is that the performance of a laboratory is improved and its working effectively controlled. An important aspect is also that the standards of quality are documented and can be demonstrated to authorities and clients. This results in an improved reputation for the laboratory (and for the institute as a whole). In short, the message is:

- say what you do
- do what you say
- do it better
- be able to show what you have done

A laboratory without accreditation performs the same tasks as a accredited company laboratory, however, the producer may trust that the results acquired during the test are reliable and repeatable.

On the other hand, independent accredited laboratories are competitive in the services' market as they possess a confirmation that they utilize the quality management system, are technically competent and are capable of producing reliable results. GLP can become confused with the standards of laboratory safety - wearing appropriate gloves, glasses and clothing to handle materials safely. GLP is a *quality system* concerned with the organisational processing process and conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported. GLP ensures the quality, integrity, and reliability of safety data.

GLP principles include:

1. Organization and Personnel
 - Management-Responsibilities
 - Sponsor-Responsibilities
 - Study Director-Responsibilities
 - Principle Investigator-Responsibilities
 - Study Personnel-Responsibilities
2. Quality assurance program
 - Quality Assurance Personnel
3. Facilities
 - Test System Facilities
 - Facilities for Test and Reference Items
4. Equipments, reagents and Materials
5. Test systems
 - Physical/Chemical
 - Biological
6. Test & Reference items
7. Standard operating procedures
8. Performance of Study
 - Study Plan
 - Conduct of Study
9. Reporting of results
10. Storage of Records and Reports

GLP and the European Union

Since 1987 the European Council had adopted two basic Directives and a Decision relating to the application of the GLP principles. Directive 2004/10/EC has replaced Directive 87/017/EEC as of 11 March 2004; Directive 2004/9/EC has replaced Directive 88/320/EEC as of 11 March 2004. (www.springerlink.com; www.spring.gov.sg/QualityStandards)

- " Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances."

This directive lays down the obligation of the Member States to designate the authorities responsible for GLP inspections in their territory. It also comprises requirements for reporting and for the internal market (i.e., mutual acceptance of data).

- "Directive 2004/9/EC of the European Parliament and of the Council of 11 February 2004 on the inspection and verification of good laboratory practice (GLP)".

The Directive requires that the OECD Revised Guides for Compliance Monitoring Procedures for GLP and the OECD Guidance for the Conduct of Test Facility Inspections and Study Audits must be followed during laboratory inspections and study audits.

At the European level, there are also 'Product Oriented Directives' referring to GLP obligations, regarding plant protection products there is Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market, which will be replaced with regulation (EC) No.1107/2009 of the European Parliament of 21 Oct, entrance in force at 15 June 2011. (www.oecd-ilibrary.org/oecd-series-)

The table below present a comparison between ISO 17025 and GLP.

<p>■ ISO Members The same standard for all ISO Designed for repetitive studies Description of Quality System in Quality Manual</p>	<p>■ OECD Members Different regulations in different countries Designed for single studies Description of Quality System in SOPs</p>
<p>General statements for responsibilities of personnel No specific requirements for storage of records and reports</p>	<p>Very specific responsibilities of personnel Specific requirements for storage, retention and archiving</p>
<p>No study plans required (standardized methods should be used) Written operating procedures without specific format</p>	<p>Study plan required for each study SOPs with detailed requirements for format and content</p>
<p>Analysis methods must be verified through inter-laboratory test (PT) Documented complaints procedures Storage of test samples and data until client accepts results</p>	<p>Validation through inter-laboratory tests not required In case of problems, only course of law Storage of test samples according to local regulatory requirements</p>

Project „*Model biological systems (and operating procedures of these model biological systems) for risk assessment of plant protection products and their active ingredients*” purposed to maintain ISO 17025 accreditation and to obtain GLP certification for the methods used in environment risk evaluation for plant protection products and their active ingredients. The maintainning of ISO 17025 accreditation and obtaining GLP certification will be possible because of the endowment of the laboratory with modern equipment to meet GLP requirements

In the mentioned project we developed the Ecotoxicology Laboratory and obtained GLP certification for four testing methods.

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