Introduction

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Content

In recent years, both basic and clinical research have joined their efforts to translate scientific discoveries into practice, from bench to bedside applications. Therefore a rapidly increasing number of laboratories are now establishing the molecular technologies to be used both in a clinical and a translational research setting. This results in an obvious need for standardization and harmonization of the developed test systems and of the laboratory procedures among different institutions.

Good Laboratory Practice (GLP) generally refers to a quality system concerned with the organizational process and the conditions under which studies are planned, performed, monitored, recorded, archived, and reported. The main goal of this system is to ensure the consistency and reliability of the results and therefore their mutual acceptance among all countries [1]. To this regard, many regulatory and guidance materials have been developed over time by governmental authorities and by accrediting or nonaccrediting organizations.

A first set of regulatory standards was developed in the late 1970s by the Organization for Economic Cooperation and Development (OECD) and by the Food and Drug Administration (FDA) [2] for assessing chemicals and testing safety of chemical products, including pharmaceuticals. The OECD standards, reviewed in 1997, dealt with a set of core elements including organization, quality assurance, facilities, test systems, controls, study design, and reporting of results relevant to nonclinical health and environmental safety studies (Table 50.1) [1]. Almost in the same time frame, the International Organization for Standardization (ISO) extended the applicability of GLP to laboratories performing clinical analysis (ISO/DIS 15189:1998, Quality Management in the

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G. Stanta (ed.), *Guidelines for Molecular Analysis in Archive Tissues*,
DOI: 10.1007/978-3-642-17890-0_50, © Springer-Verlag Berlin Heidelberg 2011

Table 50.1 GLP and GCLP core elements

GLP[a]	GCLP[b]
Organization and personnel.	Organization and personnel.
Defines management-, sponsor-, study director-, principle investigator- and personnel- responsibilities	Defines responsibilities, job description, training, competency assessments, performance evaluation, and education programme for all the personnel.
Quality assurance programme.	Quality control programme.
Responsibilities of the quality assurance personnel related to study conduction, facilities adequacy, and process compliance to GLP.	Procedures for monitoring: test standards and controls, reagents, specimens, review of QC data, QC logs, and inventory.
c	Verification of performance specifications. Standards for assay validation in clinical trials.
Facilities.	Physical facilities.
Definition of facilities for testing, for sample and reference items storage, for waste disposal, for archives.	Requirements for equipment placement, workplace environment, work areas.
Apparatus, materials, and reagents.	Equipment, materials, and reagents.
Standards for equipment maintenance and inspection, reagents labeling and storage.	Standards for equipment maintenance and inspection. Requirements for reagents and reference material verification, labeling and storage.
Test systems; test and reference items. Standards for test systems and controls handling, verification, labeling, and storage.	See "Quality control programme" and "Equipment, material, and reagents" core elements.
Standard operating procedures.	Standard operating procedures.
Guidelines for SOP writing and applicability.	Guidelines for SOP writing and applicability.
Performance of study.	Planning and conduct.
Definition of the study plan and conduct of study.	Definition of the study plan and conduct of study.
c	Specimen transport and management. Required activities for collection, transportation, and receipt.
c	Personnel safety. Required activities, equipment, and training.
Reporting. Retention of records.	Records and reports.
Requirements for reporting of results and for retention of records.	Requirements for reporting of results and for archiving reports. Standards for laboratory information system.

Elements described especially according to [a]OECD 1997 guidelines [1] and FDA's 21 CFR part.58 [10];
[b]ISO 15189 [4], CLIA [11], CAP [19], and BARQA [12].
[c]The topic has not been adequately described

Medical Laboratory). This standard introduced guidelines on specimen management, personnel safety, and verification of performance (mainly based on the ISO 17025:1999, the generic standard for testing and calibration laboratories), as core elements of the GLP. Currently, the ISO 15189 and 17025 guidelines are still relevant to all general clinical chemistry laboratories, and compliance to their standards is required for laboratory accreditation [3–5]. However, the ever-growing demand for molecular genetic testing still awaits coverage from ISO standards [6]. A draft of the best practice guidelines addressing testing for

inherited disorders was developed by the European Molecular Genetics Quality Network (EMQN) in 2001 [7] and the draft for quality assurance in genetic testing was finally issued by OECD in 2006 [6]. Importantly, this latter draft recognized that research laboratories play a pivotal role in providing tests for genetic disorders, and supplied guidance standards for the validation and translation into clinical practice of new tests.

Particular surveillance and standardization are needed by activities of laboratories that perform the analysis or evaluation of samples collected as part of a clinical trial. In 1997, the European Medicine Agency (EMEA) introduced a set of regulatory elements concerning ethical and scientific quality standards for designing, conducting, recording, and reporting trials that involve the participation of human subjects (Good Clinical Practice, GCP) [8]. More recently, GCP was recognized as too vague with respect to sample analysis to ensure practical implementation in clinical trials [9]. Consequently, GCP was implemented with applicable portions of GLP and ISO 15189 standards [4, 10] by the joined effort of the British Association of Research Quality Assurance (BARQA) and USA governmental authorities [11, 12]. This resulted in the creation of the hybrid Good Clinical Laboratory Practice (GCLP) guidelines, which allowed connecting activities of basic research and clinical research laboratories (Table 50.1) [13–15].

To date, many relevant fields are still waiting for dedicated protocols from GLP standards. For example, only peculiar branches of basic and translational molecular research on human archive tissues have been addressed so far. Among these, requirements for biospecimen resource centers were formalized by OECD and NCI in 2007 [16, 17]. Although these guidelines recognize that the reliability of data from molecular assays is heavily dependent on the quality and consistency of the analyzed biospecimens, they do not specify in detail the technical requirements for preanalytical managing of tissues [18]. Many other relevant issues of translational research, such as RNA testing and proteomics, do not benefit from dedicated items in current international standards. This is even more important because, in our experience, standardization of the methods by commercial kits is not sufficient to guarantee reproducibility; good laboratory practice is absolutely necessary to obtain reliable results [20].

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