Good Laboratory Practices and the ISO 9001:2000 standards

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ABSTRACT

The interaction between Good Laboratory Practices (GLP) and Quality Management Systems is not conflicting or exclusive but rather synergic -regardless of the specific environment in which they are applied-, since the general requirements of QMS Quality Systems lead to the compliance with the specific requirements of GLP. The purpose of this paper is to combine the specific requirements of GLPQC with those of the ISO 9001:2000 standards to obtain a Quality Management System with an adequate complementation through resource optimization, efficiency and efficacy. An analysis of both documents showed similarities between their requirements, stemming mainly from their shared goals: to establish the principles and requirements for an appropriate level of quality assurance. Most of the requirements of the GLPQC are included within ISO 9001:2000 with the exception of some specific cases, which enabled the combination of GLP and the Quality Systems as a whole. We conclude that it is convenient to integrate the specific requirements of GLP with ISO 9001:2000 guidelines to create a QMS that takes advantage of the wide-reaching, comprehensive and systemic nature of the latter, leading to better compliance with GLP, while leading to higher levels of organization and efficiency as the cornerstone for increasing customer satisfaction and preserving the competitive advantage of the entity.

Keywords: ISO 9001:2000, Good Laboratory Practices

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RESUMEN

Buenas Prácticas de Laboratorio y las normas ISO 9001: 2000. La relación entre las Buenas Prácticas de Laboratorio (BPL) y el Sistema de Gestión de la Calidad (SGC) no es antagónica ni excluyente, por el contrario, tiene un efecto sinérgico, cualquiera que sea el ámbito de aplicación, puesto que los requisitos generales del SGC contribuyen a garantizar que se cumplan los requisitos de las BPL específicas. Este trabajo tiene como objetivo integrar los requisitos específicos de las Buenas Prácticas de Laboratorio de Control de Calidad (BPLCM) y las normas ISO 9001:2000 (de la International Organisation for Standardization, en inglés, Organización Internacional de Normalización), con un SGC para una adecuada complementación, a favor de la optimización de los recursos, la eficiencia y la eficacia. Tras el análisis de ambos documentos, se distinguió una relación de similitud entre los requisitos que plantean, en lo esencial, debido a que su finalidad es establecer los principios con los que se debe trabajar en aras de conseguir un nivel adecuado de aseguramiento de la calidad. La mayoría de los requisitos de las BPLCM se hallan en las normas ISO 9001:2000, excepto algunos muy específicos, lo que posibilita conjugar las BPLCM y el SGC. Se llegó a la conclusión de que es conveniente integrar los requisitos específicos de las BPLCM y de las normas ISO 9001:2000, y crear un SGC el que se beneficie del carácter abarcador, integrador y sistémico de estas normas, que posibilite un mejor control del cumplimiento de las BPL, y a su vez, un nivel de organización y eficiencia superior, como fundamento para la satisfacción de los clientes y para la competitividad.

Palabras clave: ISO 9001:2000, Buenas Prácticas de Laboratorio

*I*ntroduction

The nineteen sixties witnessed the birth of the Good Manufacturing Practices (GMP) concept within the pharmaceutical industry, which was a consequence of a series of incidents related to drug manufacturing that ended in severe harm -including death- to consumers. GMP established the "appropriate way" to implement and perform every process involved in drug manufacturing, with the intended goal of proactively preventing any changes in the identity, safety and efficacy of pharmaceutical products [1].

The concept of Good Laboratory Practices (GLP) was first conceived within the original GMP guidelines. A whole chapter of GMP documentation was devoted to establishing the requirements to ensure the reliability of results from laboratory assays, and these principles later evolved into the current framework known as GLP.

In 1992 the National Committee for Normalization, together with the State Center for Drug Control (CECMED, according to its name in Spanish) wrote and approved the first Cuban GLP guidelines (NC-26-212) [2]. These guidelines were later revised and updated to include elements from Quality Systems that would place them in closer agreement with the latest international trends in quality management. The end result of this effort was the preparation and approval of Regulation No. 37-2004, Good Practices for Pharmaceutical Control Laboratories (GLPQC) [3], which represented a significant progress since it included concepts taken from the norms of Laboratory Quality Systems and Good Practices in general.

The fierce commercial competition typical of the current pharmaceutical industry, together with the rising technological power of this sector and the large-scale use of laboratory automation, as well the consolidation of the State as the central authority for the implementation and enforcement of pharmaceutical policies aimed at protecting an increasingly aware

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2. Norma Cubana 26-212. Buenas Prácticas de laboratorio. Comité Estatal de Normalización del MINSAP; 1992.

3. Regulación No. 37-2004. Buenas Prácticas de Laboratorios para el Control de Medicamentos. CECMED; 2004.

consumer, has turned GLP into an essential part of the operations of pharmaceutical control laboratories worldwide [4].

On the other hand, factors such as economic globalization and the deregulation of the markets, the presence and growth of new economic blocks and, especially, the increasingly demanding needs of the customers, have shown, as never before, the need for the development and implementation of quality management systems, based on the ISO 9000 standards from the International Organization for Standardization [5].

In Cuba, the Resolution of the V Congress of the Cuban Communist Party (PCC, according to its name in Spanish) stated: «the improvement of quality is ever more present among the demands imposed by developed countries». This is an accurate portrayal of the present situation, where the current mechanisms for international trade require a constant increase in the quality of Cuban manufactured good in order to successfully compete in the market. Other factors driving the implementation of quality management systems are the general requirements for entrepreneurial improvement, the enactment of Decree-Law 182 on Normalization and Quality and Decree-Law 183 on Metrology, and the implementation of the National Award for Quality of the Republic of Cuba [1].

Considering that quality control laboratories are the ultimate guarantors of the quality of industrially manufactured products, it is obvious that the proper operation of these entities is necessary for the normal course of commercial operations, business assurance, the quality of consumer goods and the prevention of economic losses. In fact, the repercussions on consumer safety provided by quality certifications granted to these laboratories often become competitive advantages, and therefore, the implementation of quality management systems in such a setting is gradually becoming an essential requirement.

This work intends to integrate the specific requirements of Good Laboratory Practices for Quality Control and the ISO 9001:2000 standards, creating a Quality Management System (QMS) that achieves the necessary level of integration to optimize the existing resources, increase efficiency and efficacy.

Development

Good Laboratory Practices

A set of rules, operating procedures and the proper practices that ensurer the reliability of the data generated by pharmaceutical control laboratories [3]

Principles, or parts, of Good Laboratory Practices:

1. Organization and personnel
2. Installations and facilities
3. Documentation
4. Equipment and instruments
5. Materials and reagents
6. Reference and assay samples
7. Assay methods. Validation
8. Self-inspections and audits
9. Quality assurance for the assays

Basic requirements of Good Laboratory Practices:

1. Norms or procedures as basic documents to establish quality standards and evaluate whether the manufactured product conforms to specifications.
2. Sampling, inspections, and testing of materials are performed by trained personnel, using appropriate methods and following established norms and procedures.
3. The samples are taken by Quality Control personnel, following approved procedures.
4. The assay methods are validated.
5. The registries and record books are kept in such a way that no data can be entered unless the described sampling or inspection/assay procedures have actually been performed. Any deviation will be carefully recorded and investigated.
6. The finished products comply with the stated specifications; and are correctly bottled and labeled.
7. The evaluation of the product includes a revision and assessment of the documentation of the process and the evaluation of any deviations.
8. The certification by authorized personnel, following previously specified procedures and requirements, is absolutely required before releasing a batch of the product.
9. Retained samples are stored following established procedures, ensuring that they are properly labeled and are kept under the specified storage conditions.
10. The Quality Control Unit is separated from the Production Unit.
11. The Quality Control personnel will be granted access to the manufacturing facilities to carry out their job.
12. The Quality Control Unit must remain under the authority of a qualified and competent person, and will have one or more laboratories equipped with all resources needed to ensure the reliability of the decisions made by Quality Control.

Quality Management Systems

The ISO 9000:2000 standards define a QMS as the management system that establishes and controls the relationship of an organization with quality.

The ISO 9001 [6] and ISO 9004 standards have been developed as a coherent pair of guidelines for Quality Management Systems, and are therefore inter-complementary. ISO 9001 specifies the requirements that must be fulfilled by a QMS and that can be used within the organizations for certification or contractual purposes; that is, it ensures customer satisfaction and guarantees efficacy. ISO 9004, on the other hand, provides blueprints for a wider range of goals, especially for the continuous improvement of performance and global efficiency, as well as for efficacy and the satisfaction of the customer and other interested parties.

The design of each system must be adapted to the specific type of organization and its particular goals and needs. It must take into account the specific goods or services provided, as well as the relationship with customers and suppliers.

Principles of a Quality Management System

Customer focus

An organization always depends on its customers; therefore, it must understand and anticipate their

4. Frederick MG. Quality Assurance Principles for Analytical Laboratories, AOAC; 1991.

5. Hrovitz J. La calidad del servicio: a la conquista del cliente. Madrid: Editorial McGraw-Hill; 1991.

6. NC-ISO 9001:2001. Sistema de Gestión de la Calidad. Requisitos; 2001.

current and future needs, satisfy their requirements and try to exceed their expectations.

Leadership

The leaders are responsible for establishing the unity of purpose and the course of an organization. The leadership must strive to create and maintain an internal environment that fosters the total involvement of the staff in achieving the goals of the organization.

Involvement of the staff

The staff is the core of an organization. Only through their commitment to the organization can the skills of the workforce be used at maximum to meet their goals.

Process approach

Any desired result can be more efficiently achieved if the necessary activities and resources are managed as a process.

System-centric management

Identifying, understanding and managing interrelated processes as a system improves the efficacy and efficiency of the work of an organization in meeting their goals.

Continuous improvement

Continually improving its global performance must be a permanent objective of an organization.

Evidence-based decision making

Efficient decisions are based on the analysis of data and information.

Mutually beneficial relationships with the suppliers

An organization and its suppliers are mutually interdependent. Therefore, a beneficial relationship between both parties increases their mutual capacity for the creation of value.

Requirements of a Quality Management System, according to the ISO 9001:2000 standards

Quality Management System

The organization must implement, document, apply, maintain and improve its quality management system. The implementation of a QMS must begin with the identification of the processes that must be managed.

Responsibilities of the administration

The administration has to commit to the development, application and improvement of the QMS, striving to convey to the staff the importance of complying with the legal and procedural requirements of the customer and establishing a quality policy. It must also strive to ensure that the goals of this policy are met, performing periodical revisions and assuring the availability of all necessary resources.

Resource management

The organization must identify and provide the necessary resources for implementing and maintaining the QMS, continuously improving its efficacy and the customer's satisfaction by complying with its requirements.

Product tailoring

The organization must plan and develop the necessary processes for tailoring the product by taking into account the interests of the customer. Therefore, it must conceive and control its design and development and define and implement purchasing processes that ensure that the acquired resources meet the specified purchasing demands, carefully selecting and evaluating the suppliers, as well as verifying the quality parameters of the acquired goods. The organization must also plan and implement the intended manufactured goods or services, controlling all follow-up and measuring devices.

Measurement, analysis and improvement

The organization must prepare and implement all follow-up, measurement and analyses procedures to prove the conformity of the product. It must also guarantee the conformity of the QMS and continuously improve its efficacy.

The advantages of a QMS are based on a clear understanding of the needs driving the change towards a new approach to quality management. These advantages are:

1. It forces the organization to define objectives, quality policies, tasks, responsibilities, assessment methods and evaluation criteria.
2. It emphasizes careful planning and a proactive approach to prevent problems, drives the implementation of periodical revisions, continuous improvement and staff training.
3. Internal improvements regarding communication, motivation and engagement, supplier assessment, the workforce's ability to change and its adaptability. Productivity
4. External improvement regarding the quality of the product, customer satisfaction, corporate image, customer reliability.
5. Decreases useless efforts, reprocessing and personnel turnover.

Integration

It follows from the study of the definition, the principles and the requirements of the GLP that they are fundamentally aligned with the principles and demands of the Quality Management Systems recommended by the ISO9001:2000 guidelines. Additionally, the latter document anticipates and recommends the integration of the QMS with other systems which are or will be implemented in the organization.

A comparison of both documents reveals that their contents are closely related, which is derived essentially from their main goal: to establish the principles and requirements for an appropriate level of quality assurance. Most of the demands of the GLPQC are already contained in the ISO 9001:2000 guidelines (*e.g.* document control, control of records, internal audits, inspection of the facilities by the management and staff), except for the more specific requirements which are carefully detailed in the GLPQC, such as those dealing with the reagents,

culture media, reference materials, certain processes –*e.g.* sterilization and filtration-, stability studies, validation, environmental monitoring of the facilities and control of the disinfectants, equipment specifications, staff hygiene, and product recall.

There are also conceptual differences and dissimilar approaches in dealing with certain topics that have a direct effect on quality, such as:

ISO	BPL
1. Establishes the documentation of the complete quality system.	1. Establishes the documentation of part of the quality system.
2. Establishes the control of both internal and external documentation, as well as that of the suppliers.	2. Establishes certain elements for the control of documentation.
3. Applicable to organizations of any kind and size.	3. Applicable only to quality control laboratories.
4. Does not place emphasis on the specificities of the facilities for handling substances.	4. Places a strong emphasis on the specific requirements of the facilities for handling substances.
5. Implemented on a voluntary basis.	5. Their implementation is mandatory.

The concept of quality improvement is not developed in Good Laboratory Practices, even though it is acknowledged (together with quality planning, assurance and control) as one of the four cornerstones of Quality Management (which are also not developed in GLP).

The ISO standards present a wider and more comprehensive view of the elements that influence the quality cycle of a product, beginning with the identification of the customer's needs and ending with the assessment of customer satisfaction, and including the processes implemented to meet the goal of continuous improvement. Although their broad applicability comes at the cost of the implicit exclusion of any details specific for a particular industry -including that privy to drug manufacturing-, ISO 9001 guidelines include the requirements for the implementation and development of efficient Quality Management Systems that can ensure an enduring compliance with the requirements of GLP.

GLP have more specific guidelines that identify the conditions needed for the development and operation of the processes related to pharmaceutical manufacturing, but with a less comprehensive approach that leaves out many vital topics which are indispensable for the efficient management of these activities and processes.

A pharmaceutical control laboratory is expected to provide valid and reliable results within a defined schedule and following specific procedures for their delivery. Preventing errors and inefficiencies, detecting and identifying the sources of errors, correcting and improving the processes and providing evidence of compliance with the requirements, are the aims of a quality system.

The topics of the control of changes and yearly checks on the product have been introduced into the quality assurance systems of the pharmaceutical industry in Cuba, and a proactive approach to error prevention is being included as a fundamental part of manufacturing processes.

It is important to stress the idea that a corporation is a single entity that works like a system formed by many systems. Therefore, many of the principles contained within the general regulations of an organization, its management methods and styles and those supporting quality management, are the basis for ensuring compliance with GLP.

The steps proposed for a simultaneous and combined approach to QMS and GLP are to:

1. Call on and obtain the commitment of the administration, which is vital for the efficient coordination of all activities and for its leadership.
2. Design a management representative.
3. Prepare work schedules, with defined stages, persons in charge, dates and estimated resources.
4. Collect and analyze the documentation which is already available at the organization.
5. Design the documentation.
6. Implement the system.
7. Check the degree of implementation.
8. Supervising and monitoring.

Conclusions

The period needed to implement a QMS in a particular laboratory will depend, to a large extent, on the commitment of the administration and its drive to engage and convince the staff on the advantages of such a decision for the organization. Implementing a QMS necessarily involves, therefore, all the human resources of the organization.

The Quality Management Systems are a new alternative for organizing labor, motivating the staff towards a continuous improvement of corporate operations and enhancing the communication between all management levels and the workforce. Such a system would thus ensure the reliability of the results of laboratory assays.

Furthermore, Quality Management Systems increase the prestige of the organization in the eyes of the customers.

It is convenient to integrate the specific requirements of GLP with the ISO 9001:2000 guidelines in order to implement a QMS that takes advantage of the more integral and systemic nature of the latter while ensuring the compliance with GLP. Such a system makes it possible to achieve higher levels of organization and efficiency as the basis for meeting the customers' satisfaction and preserving or enhancing the competitive advantage of the enterprise.

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