

Wide Concept of Quality Assurance

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Abstract: *Quality assurance (QA) is the integral segment of quality management devoted to ensuring confidence in the performance of quality. This assurance extends both internally to management and externally to clients, government agencies, regulators, certification bodies, and third parties. An alternative definition characterizes QA as the comprehensive execution of targeted and organized activities within a quality framework, documented to provide assurance that the product or service will meet the required quality. QA is all-encompassing and is not contingent on the specific requirements of the product being developed. Quality assurance (QA), quality control (QC), and good manufacturing practice (GMP) are critical considerations in the manufacturing, distribution, and marketing of pharmaceutical products, ensuring their identification, potency, purity, pharmacological safety, and efficacy. These terms are defined in various international regulatory documents, including those from the WHO, USFDA, MHRA, TGA, MCC, etc. The quality of a pharmaceutical manufacturer's products hinges on the level of adoption of QA, QC, and GMP systems throughout the production, distribution, and marketing processes over their total shelf life. The main objective of this article is to elucidate the fundamental differences between quality assurance, quality control, and good manufacturing practice (GMP), emphasizing their indispensability for pharmaceutical products. This overview delves into quality by design, identifying its elements and outlining process parameters and quality attributes for each unit operation. The advantages, opportunities, and steps involved in Quality by Design for pharmaceutical products are discussed, based on ICH guidelines Q8 for pharmaceutical development, Q9 for quality risk management, and Q10 for pharmaceutical quality systems. Additionally, the article highlights the application of Quality by Design in pharmaceutical drug development and manufacturing. This article will centre its attention on certain aspects of pharmaceutical quality systems concerning the quality assurance (QA) of produced medications. As previously noted, the eight pillars forming the basis of PQS provide a solid groundwork for further exploration.*

Keywords: Quality assurance, quality control, good manufacturing practice, good laboratory practice, quality risk management

1. Introduction

Quality Control:

Quality control (QC) within good manufacturing practice (GMP) encompasses sampling, specifications, testing, organization, documentation, and release procedures. Its primary role is to ensure that essential and pertinent tests are conducted, and materials are neither released for use nor products for sale or supply until their quality meets satisfactory standards. QC extends beyond laboratory operations, necessitating involvement in all aspects related to the product's quality. (1)

Quality control (QC) encompasses sampling, specifications, testing, documentation, and release procedures, ensuring that essential tests are conducted before materials are released for use or products for sale or supply. This extends beyond laboratory operations, involving all decisions related to product quality. It is imperative that all QC arrangements are executed effectively and reliably. The department as a whole is responsible for establishing, evaluating, validating, and implementing all QC procedures and methods. (11)

Quality control is an integral facet of quality management concentrated on meeting quality requirements. In contrast to quality assurance, which pertains to the manner in which a process is executed or a product is crafted, quality control predominantly concerns the inspection dimension of quality management. Another definition characterizes quality control as encompassing the operational techniques and activities employed to satisfy requirements for quality. (2)

Scope of quality control:

- 1) Creating specifications for raw materials, packing materials, finished products, intermediates, solvents, and reagents utilized in analyses is a crucial step.

- 2) This involves the thorough inspection, sampling, and testing of all starting materials, including packaging materials, intermediates, and finished products, following the procedures outlined in the standard operating procedures (SOPs).
- 3) Conducting stability tests to evaluate the stability of the product.
- 4) Ensuring compliance with current good manufacturing practices (cGMP) requirements for environmental conditions.
- 5) Generating analysis reports for tested samples and documenting and investigating any out of specifications (OOS) results.
- 6) Authorizing the release of product batches for sale upon verification of adherence to quality, safety, and efficacy standards.
- 7) Calibrating all laboratory instruments and devices employed in testing.
- 8) Engaging in investigations in response to market complaints regarding product quality
- 9) Scrutinizing batch manufacturing and packing records, and evaluating test reports to verify that products meet the required quality standards and have been appropriately packaged and labelled
- 10) Archiving reference samples from every market-released product batch.
- 11) Engaging in investigations in response to market complaints regarding product quality

Quality assurance:

Quality assurance is a wide ranging concept that collectively and individually influence the quality of product. Quality assurance (QA) encompasses all elements that may influence the quality of prescribed pharmaceuticals. This article specifically addresses various pharmaceutical quality systems concerning the assurance of quality in the production of medications. (11)

The expansive scope of quality assurance (QA) encompasses all factors that could potentially affect the quality of prescribed pharmaceutical products. The primary objectives of QA include ensuring the effective delivery of the intended therapeutic effect, safeguarding patients from inadvertent administration of incorrect or contaminated medications, and guaranteeing compliance with regulatory standards for pharmaceutical.

Quality assurance is the integral component of quality management focus on instilling confidence that quality requirements will be met. This confidence is dual-fold, extending internally to management and externally to customers, government agencies, regulators, certifiers, and third parties. Another definition characterizes quality assurance as encompassing all planned and systematic activities executed within the quality system, demonstrably ensuring confidence that a product or service will align with quality requirements. (12)s

Scope of QA:

- 1) Implementing sound warehousing practices to guarantee proper storage standards.
- 2) Performing checks on manufacturing processes and critical procedures.
- 3) Processing Monitoring & Control
- 4) Authorizing the final release of the drug for distribution and sale.
- 5) Conducting stability assessments and evaluating the product's shelf life.(11)
- 6) Managing the Change Control System.
- 7) Identification of out of specification
- 8) Conducting Internal Quality Audits and undertaking reviews.
- 9) Overall Inspection On manufacturing, testing operation.



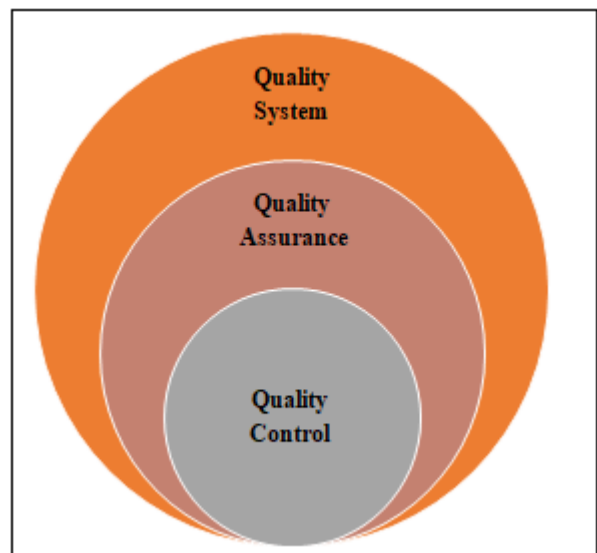
Pharmaceutical quality system:

Pharmaceutical quality systems (PQS) comprise eight foundational elements strategically crafted to yield superior final pharmaceutical products, where quality assurance (QA) and PQS collaboratively operate in synergy (depicted in Figure 1). Pharmaceutical enterprises aspire to deliver top-tier products, aiming to bolster their standing, optimize

profitability, and furnish high-quality drugs for both human and animal use. Achieving these objectives hinges on meticulously structured PQS, entailing the harmonized management of quality throughout various processes, ultimately directed at the production of the utmost quality in finished products. (4)

It is noteworthy that the European medicines agency (EMA) characterizes pharmaceutical quality systems (PQS) as the "degree of excellence processed by an item" and the act of "meeting the requirements of specific customers' needs" (as indicated by EMA, 6).

The overarching model for quality control revolves around established standards, encompassing the assessment of set standards, verification of product conformity, and the systematic incorporation of feedback into the initial system at various stages. The quality control process is integral and should be implemented across all phases of manufacturing, commencing with design and extending through raw material assembly, in-process stages, post-processing, and culminating in the evaluation of finished products, inclusive of stability testing. Quality assurance (QA) and quality control (QC) represent distinct facets of quality management, with some overlapping activities. The differentiation lies in their definitions. QA activities and responsibilities typically encompass the entirety of the quality system in various capacities, while QC functions as a subset within the broader QA framework. It's essential to note that elements within the quality system may not be explicitly addressed by QA/QC activities and responsibilities, yet they could involve both QA and QC measures.



Quality system, Quality assurance & Quality control Relationship

The implementation of a system for monitoring process performance and product quality across the entire product lifecycle is depicted in Table 1. This table showcases an optimal monitoring system that ensures the ongoing ability of processes and controls to generate a product of the desired quality while pinpointing areas for continuous improvement,

aligning with Pharmaceutical quality systems (PQS) principles. (11)

Good Laboratory Practice (GLP):

Good Laboratory Practice (GLP) constitutes a comprehensive quality system that encompasses the organizational processes and conditions governing the planning, execution, monitoring, recording, reporting, and archiving of non-clinical laboratory studies. GLP come under the Quality Assurance

In the realm of experimental research, Good Laboratory Practice (GLP) serves as a rigorous quality management system. It establishes and enforces controls within research laboratories and organizations, aiming to guarantee uniformity, consistency, reliability, reproducibility, and the overall quality and integrity of products under development for human or animal health. This comprehensive framework spans from the examination of physio-chemical properties to conducting a spectrum of non-clinical safety tests, encompassing acute to chronic toxicity assessments in fields such as pharmaceuticals. (5)

The OECD Principles of Good Laboratory Practice (GLP) are designed to facilitate the production of dependable and high-quality test data concerning the safety of industrial chemical substances and preparations. These principles have been formulated with the objective of harmonizing testing procedures to achieve the Mutual Acceptance of Data (MAD).

The distinction between GMP and GLP lies in their respective scopes. Good Manufacturing Practice is applicable across the entirety of the drug manufacturing process, whereas Good Laboratory Practice is specifically limited to the safety testing phase. Both GMP and GLP regulations are mandated and enforced by the Food and Drug Administration (FDA) in the United States. (11)

Good Manufacturing Practices (GMP):

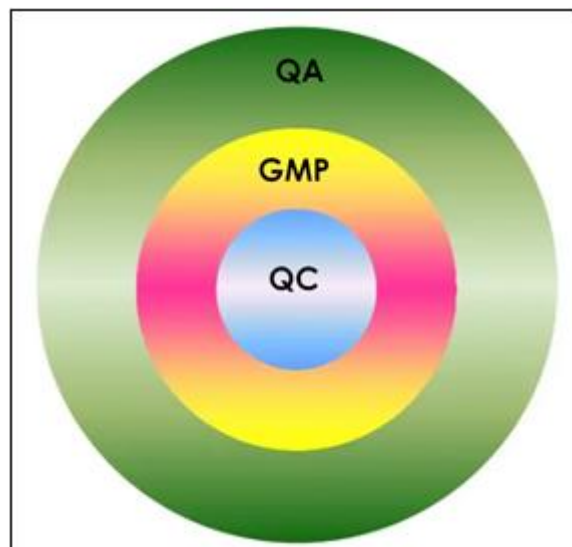
Good manufacturing practices, often denoted as 'cGMP' or 'current Good Manufacturing Practice,' constitutes a vital facet of quality assurance. Its primary objective is to secure the consistent production and meticulous control of medicinal products, adhering unwaveringly to stringent quality standards.

As per WHO guidelines, Good Manufacturing Practice (GMP) is an encompassing term that includes pharmaceutical regulations, guidelines, and directives obligatory for manufacturers in the production of medicinal products. GMP is specifically categorized under Schedule M of the Drugs and Cosmetics Act of 1940.

Under this regulatory framework:

- M1 outlines the prerequisites for factory premises dedicated to the manufacturing of homeopathic medicines.
- M2 delineates the essential requirements for factory premises engaged in the manufacture of cosmetics.
- M3 specifies the necessary conditions for factory premises involved in the manufacturing of medical devices.

Each schedule provides distinct criteria tailored to the specific nature of the products being manufactured, ensuring compliance with rigorous standards for quality and safety. (6)



Relation between QA, GMP & QC

However, discussing high-quality final pharmaceutical products is incomplete without acknowledging the significance of Good Manufacturing Practice (GMP) and Validation. It is widely recognized that every stage of manufacturing necessitates quality assurance measures for achieving favourable outcomes. The critical question then becomes: how can these measures be accomplished, and which action holds the utmost importance throughout all manufacturing stages. (11)

Solutions lie in the implementation of Good Manufacturing Practice (GMP) at each phase of the manufacturing process. GMP, an integral component of Quality Management, guarantees the consistent production and control of products, aligning with quality standards pertinent to their designated purpose and mandated by marketing authorization or product specifications. Moreover, it ensures that the produced products satisfy end-users' requirements in terms of safety, quality, and efficacy. GMP encompasses the monitoring of processes, equipment, personnel, and the environment within pharmaceutical company's. (7)

GMP is indispensable across all scenarios, spanning from initial drug trials to commercial launch. A manufacturer, aiming for optimal product quality, must establish a systematic approach to ensure consistent formulation, processing, and composition.⁴ Absent regulations in the manufacturing process, repercussions may initially go unnoticed but can later jeopardize the safety of the product. This poses a risk of harm to individuals or financial losses for the manufacturer. However, the paramount importance of patient safety serves as the impetus for companies to enhance quality and forestall unnecessary expenditure in the manufacturing process.

GMP is universally applicable to various pharmaceuticals. For instance, a 'standard product' is characterized by unit operation and risk assessment of the end product, suggesting

uncomplicated equipment and ambient conditions. However, this simplicity doesn't imply leniency; GMP should be rigorously applied, and the product manufactured following highly regimented and regulated procedures.⁴ Conversely, sterile medicines demand distinct processes and equipment, often involving biotechnology derivatives.^{4,2} These manufacturing processes introduce variability in the consistency and potency of bio-preparations, necessitating validation and continuous monitoring, while also addressing issues like purity.² Sterile manufacturing imposes more stringent requirements on equipment and necessitates specialized clean rooms. The distinctive conditions and the drug's nature often mandate additional staff training and heightened reliance on the Qualified Person (QP) for final approval. (8)

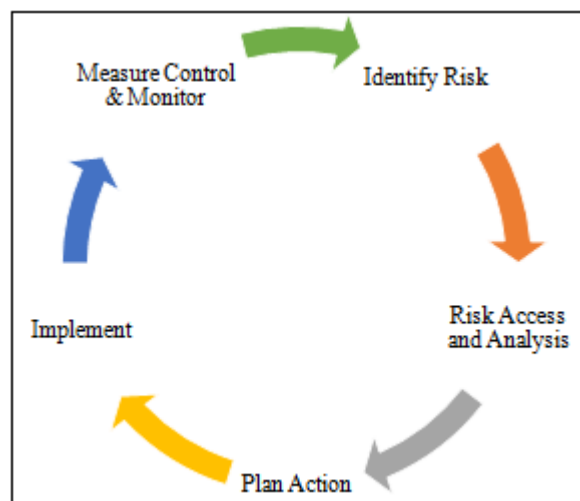
Quality Risk Management:

The Quality Risk Management system, as depicted in Figure 3, encompasses the continual monitoring and evaluation of the effectiveness of systems or procedures. This primarily entails investigating deviations that may occur at any stage of the manufacturing process and identifying additional factors, such as damaged or faulty raw materials, devices, or equipment.

The root cause analysis is not only identified but also thoroughly documented, concluding with an evaluation to affirm the attainment of quality objectives and the unaffected quality of the product.² In essence, this system is designed to safeguard product quality by addressing various issues, identifying risks, and implementing preventive measures.⁽⁹⁾

The principles of risk management extend across diverse business sectors, including the pharmaceutical industry. The manufacturing and utilization of medicinal products, along with their components, inherently involve a certain level of risk, with the risk to product quality being just one facet of the comprehensive risk landscape.⁴ A robust quality risk management program plays a pivotal role in ensuring the elevated quality of pharmaceuticals, offering a proactive mechanism for pinpointing and controlling potential quality issues throughout the development and manufacturing phases. Proficient quality risk management not only enhances regulatory confidence in a company's ability to handle potential risks but also positively influences the extent of direct regulatory oversight. (10)

Effective quality management emerges through the proper integration of quality control, quality assurance, and quality improvement endeavours. This accomplishment is realized by responding to feedback from individuals engaged in the product supply chain. A quality cycle, comprised of experts convened with the objective of enhancing manufacturing processes, environmental conditions, health, and safety, fosters improvement.^{4,6} Robust communications among the participants in the group has the potential to yield advancements surpassing routine improvements.



This guideline furnishes fundamental principles along with illustrative tools for the implementation of quality risk management across various dimensions of pharmaceutical quality. Encompassing the entire lifecycle of drug substances, drug products, and biological or biotechnological products, these aspects span development, manufacturing, distribution, inspection, and submission/review processes. The guideline's applicability extends to diverse components, including raw materials, solvents, excipients, packaging, and labelling materials, emphasizing a comprehensive approach to ensure the quality and integrity of drug (medicinal) products and biotechnological biological and products.⁽¹¹⁾

2. Summary

In pharmaceutical manufacturing, Quality Assurance (QA) serves as the benchmark to ensure that prescribed medications effectively yield the intended impact on the individual consuming them. The Pharmaceutical Quality System (PQS), an integral part of the QA framework, is purposefully devised to assist manufacturers in attaining the goal of producing high-quality finished pharmaceutical products. This achievement aligns with the requisite levels of drug regulations, ultimately ensuring efficacy and safety for patients.⁴ Key parameters for attaining these objectives include:

- 1) Designing the pharmaceutical product to meet specified needs and performance requirements.
- 2) Designing the process to consistently meet critical quality attributes of the product.
- 3) Identifying and controlling processes, equipment, personnel, and deviations appropriately.
- 4) Continuously monitoring and updating the entire manufacturing process to ensure consistent quality over time.

The application of Pharmaceutical Quality Systems in pharmaceutical products can extend to pharmaceutical development, facilitating innovation and continual improvement in prescribed medications. It serves as the tool for achieving product realization by designing, planning, implementing, maintaining, and continuously improving a system, allowing for the consistent delivery of pharmaceuticals with appropriate quality attributes.

3. Conclusion

This article will centre its attention on certain aspects of Pharmaceutical Quality Systems concerning the Quality Assurance (QA) of produced medications. As previously noted, the eight pillars forming the basis of PQS provide a solid groundwork for further exploration.

This concise overview examines global approaches to evaluating geotaxis impurities, including residual solvents and various inorganic and organic impurities, in pharmaceuticals. In response to national and international regulations, there is a growing need to not only assess the purity profile but also the impurity profile of pharmaceutical products. The discussion encompasses the significance of ensuring the quality, efficacy, and safety of pharmaceuticals, exploring aspects such as the sources, types, control, and regulatory considerations of impurities.

The reliable supply of high-quality essential medicines is crucial for the effectiveness of any country's healthcare system, as substandard medicines can pose serious risks to consumers. Even minute quantities of unwanted chemicals in a medicine can impact its efficacy and safety. Pharmaceuticals, unlike other products, are dynamic, and their properties can change from manufacturing to consumption. Consequently, global attention, particularly from regulatory authorities, is increasingly focused on ensuring the quality of pharmaceuticals.

The presence of impurities in pharmaceutical products is a significant concern, not only due to the inherent toxicity of certain contaminants but also because of their potential adverse effects on drug stability and shelf-life. Impurities in pharmaceutical and drug products refer to unwanted chemicals, including organic, inorganic, and residual solvents. These impurities may persist with the active pharmaceutical ingredients (APIs), emerge during formulation, or develop over time. Among these impurities, organic contaminants are the most frequently encountered.

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