

# A scoping review of regulatory guidelines for the assurance of medicinal product quality throughout their lifecycle

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## Introduction

Quality, defined as the degree to which a set of inherent characteristics fulfills requirements (ICH Q9; ICH Q10) remains a crucial part of regulatory framework, with many requirements and guidelines aiming the safe use of medicinal products by assuring highly qualitative products.

Many steps should be taken as measures and procedures to follow towards the realization of a product during product's lifecycle, including: Pharmaceutical Development, Technology Transfer and Commercial Manufacturing up to Products Discontinuation.

World is giving much interest to the unifying of documents preparation and applying processes, while more than 40 guidelines have been harmonized to date amongst the 3 regions: Europe, United States of America (USA) and Japan. Including the aiming of International Pharmaceutical Federation (FIP) and the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), pharmaceutical industry is considered the most regulated one for more than 50 years (Phillips et al., 2015).

Considering this complicated though important process, the main theme of this short paper is analysis of the existing guidelines for Quality, thus providing information from all aspects of pharmaceutical quality.

## Materials and methods

This scoping review provides an overview of the current state of the art within the quality requirements, guidelines, practices and standards in general, and steps taken toward continual improvement of all processes. During the process, databases and guidelines of ICH, EU,

WHO and ISO were analyzed. Additional published data were included from PubMed search engine.

Further analysis included discussion of the documents complements for the quality practices, requirements, standards, guidelines, auditing/inspection, staff responsibilities and training/education within the pharmaceutical industry and regulatory environment.

## Results and discussion

There are many components that enable the system to function in service of the main purpose of the system itself, with quality undeniably reaching the top of the list.

Development and commercial manufacturing, up to the discontinuation of pharmaceutical products are processes subjected to government regulation, review and approval of new products and site inspection for quality management of production, packaging, storage, and distribution (Xu et al., 2016). Furthermore, all these stages of the product lifecycle need an established connection in between and sophisticated control accompanied by relevant procedures, documentation, technology, and qualified staff.

The quality of a medicinal products throughout the whole lifecycle is achieved by risk-based and science-based approaches as a result of the creation of a Quality Management System (QMS) based on the International Council of Harmonization (ICH) Guidelines, Good Manufacturing Practice (GMP) certification and ISO standards.

Since 2003 when ICH developed the Quality Vision "Develop a harmonized pharmaceutical quality system applicable across the life cycle of the product emphasizing an integrated approach to quality risk management and

science” (Brussels, July 2003), several Guidelines (Q8-Q12) have been generated. ICH Quality Guidelines present the risk, approaches and principles towards qualitative product and a consistent product’s life from the initial development through marketing until the product’s discontinuation (Lifecycle Management, LCM). Requirements of Good Distribution Practice (GDP) and Good Pharmacy Practice (GMP) are also very important toward consistent integrity of product’s life.

Considering all the ICH guidelines for the quality assurance of the product during lifecycle such as ICH Q8, Q9, Q10, Q11 and the harmonization in between them, there were still some gaps existing in the terms of full realization of the benefits, which were intended to be met by the new guideline named ICH Q12. This guideline aims continual assurance of high-quality products, promote innovation and continual improvement, a transparent and efficient management of post-approval Chemistry (ICH Q12).

Pharmaceutical quality management and product lifecycle management remains crucial in terms of harmonizing the industry, assessors and inspectors, as well as providing a great benefit to the public health by enhancing the quality and availability of medicines worldwide. In a good quality system and approved compliance with local and international regulatory requirements (since pharmaceutical products and raw materials are manufactured and distributed worldwide) medicinal products will not be sold or supplied before certification that each production batch has been produced and controlled in accordance with the requirement of marketing authorization (MA) and other relevant requirement for the production, control, and product release.

A very complex system of quality, consisting of the concepts of Quality Assurance (QA), Quality Control (QC) and Quality Risk Management (QRM) must be in place.

It should be finally noted that the top 5 quality attributes that are related to management responsibility and continual improvement are (Patel et al., 2015): (i) management communication that quality is everyone’s responsibility, (ii) site has formal quality improvement objectives and targets, (iii) clear performance criteria for feedback and coaching, (iv) quality topics included in at least half of all-hands meetings, and (v) collecting error prevention metric.

Proper documentation and records is a basic system in a good pharmaceutical quality system, enhancing visibility of the quality assurance. This comes especially because it is considered that all products and processes have an inherent element of risk, enforcing manufacturers to focus on non-conformities, possible deficiencies and planning of preventive actions in order to anticipate and prevent future possible problems (Haleem et al., 2015).

## Conclusion

It is strongly believed that the concept on ICH Q12 Guideline will make possible the quality assurance of products during their full lifecycle, including stages after regulatory approval. The building of an integrated quality system from the industry will help the industry itself for the improvement toward achieving the objective of high qualitative products during the lifecycle of the product, good system documentation, measurement of performance, continual improvement, while helping the regulators for the oversight of industries and (above everything) enabling patients the usage of high qualitative products. It is of great importance that the post-approval phase should be given as much importance as pre-approval process, not just in regard to the safety but also quality of medicinal products.

The global emphasis that is given today to post-approval product lifecycle management and the changes supported by risk and science-based approaches, will help industry achieving their goals and objectives.

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