A Process Approach to Pharmaceutical Quality Systems

A Guide to ICH Q10 Compliance

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A. Pharmaceutical Quality System (ICH Q10)
Introduction

The overall aim of implementing a *Pharmaceutical Quality System* (PQS) is to continually improve the effectiveness and efficiency of the organization’s performance and thus achieve compliance with GMP regulations around the world.

A PQS must be led in a systematic and visible manner and involve people at all levels. A company performs many internal activities such as manufacturing, research, development, clinical trials, registration, marketing, purchasing, warehousing and distribution, to name but a few. Activities need to be addressed in a PQS which describes all the processes that have to be managed.

All these activities should be embedded in a life cycle approach, as laid down in ICH Q10 *Pharmaceutical Quality System* (Appendix A). The phases of a product’s lifecycle are:

- Development
- Technology Transfer
- Commercial Manufacturing
- Product Discontinuation

To implement an effective PQS, companies must break down their company into a series of processes, and take the following steps with regard to each process:

- Define the responsibilities within each process;
- Identify interfaces, within and between different processes;
- Nominate ‘process owners’ for the processes identified;
- Establish Key Performance Indicators (KPIs) for measuring the effectiveness of a process and thus the value it brings to the company; and
- Implement routine assessments of process performance and identification of potential improvements.

A PQS requires the systematic involvement of senior management in the functioning and success of a PQS. In practice, senior management directs the organization towards its quality objectives by:

- determining responsibilities within the organization (global, regional, local),
- providing sufficient resources (infrastructure – e.g. offices, manufacturing, IT – time and personnel) to support the processes,
- defining information and communication flow at all levels of the organization,
- integrating the concept of Quality Risk management at all levels of the organization,
- implementing a concept of Knowledge Management,
- fostering all initiatives that lead to improved process robustness (production processes as well as business processes),
• encouraging the implementation of concepts that will enable continual improvement at all levels, and

• using the (regular) Management Review to direct the PQS and thus the organization.

It must be stressed that outsourced operations and related activities also need to be covered by the PQS.
Documentation

A documentation system remains a fundamental component of a PQS. The objective of such documentation is to identify and describe what needs to be in place. It is an essential tool to keep all processes in a state of control and it must satisfy GMP requirements.

Senior management defines the documentation that is required to run a PQS and support effective and efficient operation of the processes.

It basically encompasses:

- a statement of senior management’s commitment to quality,
- a quality manual,
- documented procedures, and
- records documenting operations, KPI monitoring, reviews and quality improvements.

GMP documentation, especially regarding Master Production Instructions and laboratory documentation, provides detailed information as laid down in the respective regulations. GMP requirements need to be reflected in the PQS for reasons of compliance.

The documentation created to run a PQS and to comply with GMP requirements should fulfill criteria with respect to:

- functionality,
- user-friendliness,
- the structure of the company’s documentation system,
- knowledge management, and
- interfaces between departments.

Documentation may be available in any form or media, such as paper, micro-fiche, electronic (CD/DVD) etc., suitable to needs.

In a GMP environment, quality-related activities are to be recorded at the time that they are performed.

Deviations from established procedures need to be documented and explained and/or investigated: a complaint and recall procedure has to be in place.

Contract manufacturing (including laboratories) needs to be carefully managed, e.g. through evaluation, assessment and documentation (including a quality agreement). All (GMP) activities and responsibilities have to be defined in writing.

Quality Manual

The central document of a PQS is the Quality Manual. Although it is a company’s decision how detailed this should be, the quality manual should be made as comprehensive as practical.
The main elements to be incorporated include:

- the scope of the PQS,
- senior management’s quality commitment,
- a description of the main processes,
- their interactions, and
- the description of major responsibilities.

**Control of documents**

All documents and records required by the PQS are subject to appropriate control. A documented procedure needs to be established to define the following controls:

- Drafting, review, approval (Quality Unit at minimum for GMP-related documents) and updating of documents,
- Handling and control of changes to documents (version control) including P & ID (Piping & Instrumentation Diagram) schemes,
- Handling, control and internal distribution of external documents, and
- Withdrawal and prevention of unintended use of obsolete documents.

**Control of records**

Records provide evidence of conformity to requirements. They should be legible, readily identifiable and retrievable. A documented procedure should define the control needed for identification, storage, protection, retrieval, retention time and disposition of records.

The control of records includes hard copies as well as electronically-stored data.

Records should be established, at least for raw materials, intermediates, labeling, packaging materials, batch production, laboratory data (including Certificates of Analysis and stability data), calibration, distribution, complaints and returns.

A procedure for the review of batch production and laboratory records is required (batch record review).
Elements of a PQS

Specific GMP requirements of the pharmaceutical industry can be categorized and incorporated into a PQS. The four main processes of a PQS are: Management Responsibility, Resource Management, Manufacturing Operations and Evaluation Activities. All GMP requirements can be assigned to one of these processes.

Management responsibility

Leadership, commitment and the active involvement of senior management are essential to the effective functioning of the PQS.

Senior management should provide evidence of its commitment to the development and implementation of the PQS by taking the following steps:

- Communicating the importance of meeting patient needs as well as regulatory (GMP) and legal requirements, including environmental, health and safety requirements,
- Ensuring that employees have knowledge of the regulatory requirements,
- Establishing quality policy,
- Ensuring that quality objectives are established,
- Defining responsibilities,
- Fostering continual improvement,
- Defining methods to measure the organization’s performance,
- Conducting regular management reviews, and
- Ensuring the availability of sufficient resources (manpower, time and infrastructure).

Quality policy

One main purpose of the quality policy is that it demonstrates senior management’s commitment to quality and to the provision of adequate resources, both to the employees of the company and to outsiders. It is management’s vehicle for establishing quality expectations, and should include the following elements:

- It should stress the importance of compliance with regulatory/GMP requirements and continuous quality improvement;
- It should establish measures that will be used to ensure that the quality policy is being enacted in day-to-day business; and
- It should be communicated to employees at all levels within the organization, stressing that all individuals involved in a process are responsible for its quality.