
Guidance for Industry

Q10 Pharmaceutical Quality System

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)**

**April 2009
ICH**

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Q10 Pharmaceutical Quality System

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TABLE OF CONTENTS

I. INTRODUCTION (1, 1.1)..... 1

II. PHARMACEUTICAL QUALITY MANAGEMENT SYSTEM..... 2

A. Scope (1.2)..... 2

**B. Relationship of ICH Q10 to Regional GMP Requirements, ISO Standards,
 and ICH Q7 (1.3)..... 3**

C. Relationship of ICH Q10 to Regulatory Approaches (1.4)..... 3

D. ICH Q10 Objectives (1.5) 3

E. Enablers: Knowledge Management and Quality Risk Management (1.6) 4

F. Design and Content Considerations (1.7) 4

G. Quality Manual (1.8)..... 5

III. MANAGEMENT RESPONSIBILITY (2)..... 5

A. Management Commitment (2.1)..... 5

B. Quality Policy (2.2)..... 6

C. Quality Planning (2.3)..... 6

D. Resource Management (2.4)..... 7

E. Internal Communication (2.5) 7

F. Management Review (2.6) 7

G. Management of Outsourced Activities and Purchased Materials (2.7)..... 7

H. Management of Change in Product Ownership (2.8) 8

**IV. CONTINUAL IMPROVEMENT OF PROCESS PERFORMANCE AND
PRODUCT QUALITY (3) 8**

A. Lifecycle Stage Goals (3.1) 8

B. Pharmaceutical Quality System Elements (3.2) 9

**V. CONTINUAL IMPROVEMENT OF THE PHARMACEUTICAL QUALITY
SYSTEM (4) 13**

A. Management Review of the Pharmaceutical Quality System (4.1)..... 13

**B. Monitoring of Internal and External Factors That Can Have an Impact on the
 Pharmaceutical Quality System (4.2) 13**

C. Outcomes of Management Review and Monitoring (4.3)..... 14

VI. GLOSSARY (5)..... 15

**Annex I: Potential Opportunities To Enhance Science- and Risk-Based Regulatory
Approaches * 18**

Annex 2: Diagram of the ICH Q10 Pharmaceutical Quality System Model.....19

Guidance for Industry¹

Q10 Pharmaceutical Quality System

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I. INTRODUCTION (1, 1.1)²

This internationally harmonized guidance is intended to assist pharmaceutical manufacturers by describing a model for an effective *quality* management system for the pharmaceutical industry, referred to as the *pharmaceutical quality system*. Throughout this guidance, the term *pharmaceutical quality system* refers to the ICH Q10 model.

ICH Q10 describes one comprehensive model for an effective pharmaceutical quality system that is based on International Organization for Standardization (ISO) quality concepts, includes applicable good manufacturing practice (GMP) regulations, and complements ICH “Q8 Pharmaceutical Development” and ICH “Q9 Quality Risk Management.”³ ICH Q10 is a model for a pharmaceutical quality system that can be implemented throughout the different stages of a product lifecycle. Much of the content of ICH Q10 applicable to manufacturing sites is currently specified by regional GMP requirements. ICH Q10 is not intended to create any new expectations beyond current regulatory requirements. Consequently, the content of ICH Q10 that is additional to current regional GMP requirements is optional.

¹ This guidance was developed within the Expert Working Group (Quality) of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and has been subject to consultation by the regulatory parties, in accordance with the ICH process. This document has been endorsed by the ICH Steering Committee at *Step 4* of the ICH process, June 2008. At *Step 4* of the process, the final draft is recommended for adoption to the regulatory bodies of the European Union, Japan, and the United States.

² Arabic numbers reflect the organizational breakdown of the document endorsed by the ICH Steering Committee at *Step 4* of the ICH process, June 2008.

³ These guidances are available on the Internet at <http://www.fda.gov/cder/guidance/index.htm>. We update guidances periodically. To make sure you have the most recent version of a guidance, check the CDER guidance page at <http://www.fda.gov/cder/guidance/index.htm>

ICH Q10 demonstrates industry and regulatory authorities' support of an effective pharmaceutical quality system to enhance the quality and availability of medicines around the world in the interest of public health. Implementation of ICH Q10 throughout the product lifecycle should facilitate *innovation* and *continual improvement* and strengthen the link between pharmaceutical development and manufacturing activities.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. PHARMACEUTICAL QUALITY MANAGEMENT SYSTEM

A. Scope (1.2)

This guidance applies to the systems supporting the development and manufacture of pharmaceutical drug substances (i.e., active pharmaceutical ingredients (APIs)) and drug products, including biotechnology and biological products, throughout the product lifecycle.

The elements of ICH Q10 should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognizing the differences among, and the different goals of, each stage (see section IV (3)).

For the purposes of this guidance, the product lifecycle includes the following technical activities for new and existing products:

- Pharmaceutical Development
 - Drug substance development
 - Formulation development (including container/closure system)
 - Manufacture of investigational products
 - Delivery system development (where relevant)
 - Manufacturing process development and scale-up
 - Analytical method development
- Technology Transfer
 - New product transfers during development through manufacturing
 - Transfers within or between manufacturing and testing sites for marketed products
- Commercial Manufacturing
 - Acquisition and control of materials
 - Provision of facilities, utilities, and equipment
 - Production (including packaging and labeling)
 - Quality control and assurance
 - Release
 - Storage

- Distribution (excluding wholesaler activities)
- Product Discontinuation
 - Retention of documentation
 - Sample retention
 - Continued product assessment and reporting

B. Relationship of ICH Q10 to Regional GMP Requirements, ISO Standards, and ICH Q7 (1.3)

Regional GMP requirements, the ICH guidance “Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients,” and ISO quality management system guidelines form the foundation for ICH Q10. To meet the objectives described below, ICH Q10 augments GMPs by describing specific quality system elements and management responsibilities. ICH Q10 provides a harmonized model for a pharmaceutical quality system throughout the lifecycle of a product and is intended to be used together with regional GMP requirements.

The regional GMPs do not explicitly address all stages of the product lifecycle (e.g., development). The quality system elements and management responsibilities described in this guidance are intended to encourage the use of science- and risk-based approaches at each lifecycle stage, thereby promoting continual improvement across the entire product lifecycle.

C. Relationship of ICH Q10 to Regulatory Approaches (1.4)

Regulatory approaches for a specific product or manufacturing facility should be commensurate with the level of product and process understanding, the results of *quality risk management*, and the effectiveness of the pharmaceutical quality system. When implemented, the effectiveness of the pharmaceutical quality system can normally be evaluated during a regulatory inspection at the manufacturing site. Potential opportunities to enhance science- and risk-based regulatory approaches are identified in Annex 1. Regulatory processes will be determined by region.

D. ICH Q10 Objectives (1.5)

Implementation of the Q10 model should result in achievement of three main objectives that complement or enhance regional GMP requirements.

*1. Achieve **Product Realization** (1.5.1)*

To establish, implement, and maintain a system that allows the delivery of products with the quality attributes appropriate to meet the needs of patients, health care professionals, regulatory authorities (including compliance with approved regulatory filings) and other internal and external customers.

*2. Establish and Maintain a **State of Control** (1.5.2)*

To develop and use effective monitoring and control systems for process performance and product quality, thereby providing assurance of continued suitability and *capability of processes*. Quality risk management can be useful in identifying the monitoring and control systems.

3 *Facilitate Continual Improvement (1.5.3)*

To identify and implement appropriate product quality improvements, process improvements, variability reduction, innovations, and pharmaceutical quality system enhancements, thereby increasing the ability to fulfill a pharmaceutical manufacturer's own quality needs consistently. Quality risk management can be useful for identifying and prioritizing areas for continual improvement.

E. Enablers: Knowledge Management and Quality Risk Management (1.6)

Use of *knowledge management* and quality risk management will enable a company to implement ICH Q10 effectively and successfully. These enablers will facilitate achievement of the objectives described in section II.D (1.5) above by providing the means for science- and risk-based decisions related to product quality.

1. *Knowledge Management (1.6.1)*

Product and process knowledge should be managed from development through the commercial life of the product up to and including product discontinuation. For example, development activities using scientific approaches provide knowledge for product and process understanding. Knowledge management is a systematic approach to acquiring, analyzing, storing, and disseminating information related to products, manufacturing processes, and components. Sources of knowledge include, but are not limited to, prior knowledge (public domain or internally documented); pharmaceutical development studies; technology transfer activities; process validation studies over the product lifecycle; manufacturing experience; innovation; continual improvement; and *change management* activities.

2. *Quality Risk Management (1.6.2)*

Quality risk management is integral to an effective pharmaceutical quality system. It can provide a proactive approach to identifying, scientifically evaluating, and controlling potential risks to quality. It facilitates continual improvement of process performance and product quality throughout the product lifecycle. ICH Q9 provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality.

F. Design and Content Considerations (1.7)

- (a) The design, organization, and documentation of the pharmaceutical quality system should be well structured and clear to facilitate common understanding and consistent application.
- (b) The elements of ICH Q10 should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognizing the different goals

and knowledge available for each stage.

- (c) The size and complexity of the company's activities should be taken into consideration when developing a new pharmaceutical quality system or modifying an existing one. The design of the pharmaceutical quality system should incorporate appropriate risk management principles. While some aspects of the pharmaceutical quality system can be company wide and others site specific, the effectiveness of the pharmaceutical quality system is normally demonstrated at the site level.
- (d) The pharmaceutical quality system should include appropriate processes, resources, and responsibilities to provide assurance of the quality of *outsourced activities* and purchased materials as described in section III.G (2.7).
- (e) Management responsibilities, as described in section III (2), should be identified within the pharmaceutical quality system.
- (f) The pharmaceutical quality system should include the following elements, as described in section IV (3): process performance and product quality monitoring, *corrective* and *preventive action*, change management, and management review.
- (g) *Performance indicators*, as described in section V (4), should be identified and used to monitor the effectiveness of processes within the pharmaceutical quality system.

G. Quality Manual (1.8)

A *Quality Manual* or equivalent documentation approach should be established and should contain the description of the pharmaceutical quality system. The description should include:

- (a) The *quality policy* (see section III (2)).
- (b) The scope of the pharmaceutical quality system.
- (c) Identification of the pharmaceutical quality system processes, as well as their sequences, linkages, and interdependencies. Process maps and flow charts can be useful tools to facilitate depicting pharmaceutical quality system processes in a visual manner.
- (d) Management responsibilities within the pharmaceutical quality system (see section III (2)).

III. MANAGEMENT RESPONSIBILITY (2)

Leadership is essential to establish and maintain a company-wide commitment to quality and for the performance of the pharmaceutical quality system.

A. Management Commitment (2.1)

- (a) *Senior management* has the ultimate responsibility to ensure an effective pharmaceutical quality system is in place to achieve the *quality objectives*, and that

roles, responsibilities, and authorities are defined, communicated, and implemented throughout the company.

(b) Management should:

- (1) Participate in the design, implementation, monitoring, and maintenance of an effective pharmaceutical quality system.
- (2) Demonstrate strong and visible support for the pharmaceutical quality system and ensure its implementation throughout their organization.
- (3) Ensure a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management.
- (4) Define individual and collective roles, responsibilities, authorities, and inter-relationships of all organizational units related to the pharmaceutical quality system. Ensure these interactions are communicated and understood at all levels of the organization. An independent quality unit/structure with authority to fulfill certain pharmaceutical quality system responsibilities is required by regional regulations.
- (5) Conduct management reviews of process performance and product quality and of the pharmaceutical quality system.
- (6) Advocate continual improvement.
- (7) Commit appropriate resources.

B. Quality Policy (2.2)

- (a) Senior management should establish a quality policy that describes the overall intentions and direction of the company related to quality.
- (b) The quality policy should include an expectation to comply with applicable regulatory requirements and should facilitate continual improvement of the pharmaceutical quality system.
- (c) The quality policy should be communicated to and understood by personnel at all levels in the company.
- (d) The quality policy should be reviewed periodically for continuing effectiveness.

C. Quality Planning (2.3)

- (a) Senior management should ensure the quality objectives to implement the quality policy are defined and communicated.
- (b) Quality objectives should be supported by all relevant levels of the company.
- (c) Quality objectives should align with the company's strategies and be consistent with the quality policy.
- (d) Management should provide the appropriate resources and training to achieve the

quality objectives.

- (e) Performance indicators that measure progress against quality objectives should be established, monitored, communicated regularly, and acted upon as appropriate as described in section V.A (4.1) of this document.

D. Resource Management (2.4)

- (a) Management should determine and provide adequate and appropriate resources (human, financial, materials, facilities, and equipment) to implement and maintain the pharmaceutical quality system and continually improve its effectiveness.
- (b) Management should ensure that resources are appropriately applied to a specific product, process, or site.

E. Internal Communication (2.5)

- (a) Management should ensure appropriate communication processes are established and implemented within the organization.
- (b) Communications processes should ensure the flow of appropriate information between all levels of the company.
- (c) Communication processes should ensure the appropriate and timely escalation of certain product quality and pharmaceutical quality system issues.

F. Management Review (2.6)

- (a) Senior management should be responsible for pharmaceutical quality system governance through management review to ensure its continuing suitability and effectiveness.
- (b) Management should assess the conclusions of periodic reviews of process performance and product quality and of the pharmaceutical quality system, as described in sections IV (3) and V (4).

G. Management of Outsourced Activities and Purchased Materials (2.7)

The pharmaceutical quality system, including the management responsibilities described in this section, extends to the control and review of any outsourced activities and quality of purchased materials. The pharmaceutical company is ultimately responsible to ensure processes are in place to assure the control of outsourced activities and quality of purchased materials. These processes should incorporate quality risk management and include:

- (a) Assessing prior to outsourcing operations or selecting material suppliers, the suitability and competence of the other party to carry out the activity or provide the material

using a defined supply chain (e.g., audits, material evaluations, qualification).

- (b) Defining the responsibilities and communication processes for quality-related activities of the involved parties. For outsourced activities, this should be included in a written agreement between the contract giver and contract acceptor.
- (c) Monitoring and review of the performance of the contract acceptor or the quality of the material from the provider, and the identification and implementation of any essential improvements.
- (d) Monitoring incoming ingredients and materials to ensure they are from approved sources using the agreed supply chain.

H. Management of Change in Product Ownership (2.8)

When product ownership changes (e.g., through acquisitions), management should consider the complexity of this and ensure:

- (a) The ongoing responsibilities are defined for each company involved
- (b) The essential information is transferred

IV. CONTINUAL IMPROVEMENT OF PROCESS PERFORMANCE AND PRODUCT QUALITY (3)

This section describes the lifecycle stage goals and the four specific pharmaceutical quality system elements that augment regional requirements to achieve the ICH Q10 objectives, as defined in section II.D (1.5). It does not restate all regional GMP requirements.

A. Lifecycle Stage Goals (3.1)

The goals of each product lifecycle stage are described below.

1. Pharmaceutical Development (3.1.1)

The goal of pharmaceutical development activities is to design a product and its manufacturing process to consistently deliver the intended performance and meet the needs of patients and healthcare professionals, and regulatory authorities and internal customers' requirements. Approaches to pharmaceutical development are described in ICH Q8. The results of exploratory and clinical development studies, while outside the scope of this guidance, are inputs to pharmaceutical development.

2. Technology Transfer (3.1.2)

The goal of technology transfer activities is to transfer product and process knowledge between development and manufacturing, and within or between manufacturing sites to achieve product

realization. This knowledge forms the basis for the manufacturing process, *control strategy*, process validation approach, and ongoing continual improvement.

3. *Commercial Manufacturing (3.1.3)*

The goals of manufacturing activities include achieving product realization, establishing and maintaining a state of control, and facilitating continual improvement. The pharmaceutical quality system should assure that the desired product quality is routinely met, suitable process performance is achieved, the set of controls are appropriate, improvement opportunities are identified and evaluated, and the body of knowledge is continually expanded.

4. *Product Discontinuation (3.1.4)*

The goal of product discontinuation activities is to manage the terminal stage of the product lifecycle effectively. For product discontinuation, a predefined approach should be used to manage activities such as retention of documentation and samples and continued product assessment (e.g., complaint handling and stability) and reporting in accordance with regulatory requirements.

B. Pharmaceutical Quality System Elements (3.2)

The elements described below might be required in part under regional GMP regulations. However, the Q10 model's intent is to enhance these elements to promote the lifecycle approach to product quality. These four elements are:

- Process performance and product quality monitoring system
- *Corrective action* and *preventive action* (CAPA) system
- Change management system
- Management review of process performance and product quality

These elements should be applied in a manner that is appropriate and proportionate to each of the product lifecycle stages, recognizing the differences among the stages and the different goals of each stage. Throughout the product lifecycle, companies are encouraged to evaluate opportunities for innovative approaches to improve product quality.

Each element is followed by a table of example applications of the element to the stages of the pharmaceutical lifecycle.

1. *Process Performance and Product Quality Monitoring System 3.2.1*

Pharmaceutical companies should plan and execute a system for the monitoring of process performance and product quality to ensure a state of control is maintained. An effective monitoring system provides assurance of the continued capability of processes and controls to produce a product of desired quality and to identify areas for continual improvement. The process performance and product quality monitoring system should:

- (a) Use quality risk management to establish the control strategy. This can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. The control strategy should facilitate timely *feedback/feedforward* and appropriate corrective action and preventive action.
- (b) Provide the tools for measurement and analysis of parameters and attributes identified in the control strategy (e.g., data management and statistical tools).
- (c) Analyze parameters and attributes identified in the control strategy to verify continued operation within a state of control.
- (d) Identify sources of variation affecting process performance and product quality for potential continual improvement activities to reduce or control variation.
- (e) Include feedback on product quality from both internal and external sources (e.g., complaints, product rejections, nonconformances, recalls, deviations, audits and regulatory inspections, and findings).
- (f) Provide knowledge to enhance process understanding, enrich the *design space* (where established), and enable innovative approaches to process validation.

Table I: Application of Process Performance and Product Quality Monitoring System Throughout the Product Lifecycle

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Process and product knowledge generated and process and product monitoring conducted throughout development can be used to establish a control strategy for manufacturing.	Monitoring during scale-up activities can provide a preliminary indication of process performance and the successful integration into manufacturing. Knowledge obtained during transfer and scale-up activities can be useful in further developing the control strategy.	A well-defined system for process performance and product quality monitoring should be applied to assure performance within a state of control and to identify improvement areas.	Once manufacturing ceases, monitoring such as stability testing should continue to completion of the studies. Appropriate action on marketed product should continue to be executed according to regional regulations.

2. *Corrective Action and Preventive Action (CAPA) System (3.2.2)*

The pharmaceutical company should have a system for implementing corrective actions and preventive actions resulting from the investigation of complaints, product rejections, nonconformances, recalls, deviations, audits, regulatory inspections and findings, and trends from process performance and product quality monitoring. A structured approach to the

investigation process should be used with the objective of determining the root cause. The level of effort, formality, and documentation of the investigation should be commensurate with the level of risk, in line with ICH Q9. CAPA methodology should result in product and process improvements and enhanced product and process understanding.

Table II: Application of Corrective Action and Preventive Action System Throughout the Product Lifecycle

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Product or process variability is explored. CAPA methodology is useful where corrective actions and preventive actions are incorporated into the iterative design and development process.	CAPA can be used as an effective system for feedback, feedforward, and continual improvement.	CAPA should be used, and the effectiveness of the actions should be evaluated.	CAPA should continue after the product is discontinued. The impact on product remaining on the market should be considered, as well as other products that might be affected.

3. *Change Management System (3.2.3)*

Innovation, continual improvement, the outputs of process performance and product quality monitoring, and CAPA drive change. To evaluate, approve, and implement these changes properly, a company should have an effective change management system. There is generally a difference in formality of change management processes prior to the initial regulatory submission and after submission, where changes to the regulatory filing might be required under regional requirements.

The change management system ensures continual improvement is undertaken in a timely and effective manner. It should provide a high degree of assurance there are no unintended consequences of the change.

The change management system should include the following, as appropriate for the stage of the lifecycle:

- (a) Quality risk management should be utilized to evaluate proposed changes. The level of effort and formality of the evaluation should be commensurate with the level of risk.
- (b) Proposed changes should be evaluated relative to the marketing authorization, including design space, where established, and/or current product and process understanding. There should be an assessment to determine whether a change to the regulatory filing is required under regional requirements. As stated in ICH Q8, working within the design space is not considered a change (from a regulatory filing perspective). However, from a pharmaceutical quality system standpoint, all changes should be evaluated by a company’s change management system.
- (c) Proposed changes should be evaluated by expert teams contributing the appropriate

expertise and knowledge from relevant areas (e.g., Pharmaceutical Development, Manufacturing, Quality, Regulatory Affairs, and Medical) to ensure the change is technically justified. Prospective evaluation criteria for a proposed change should be set.

- (d) After implementation, an evaluation of the change should be undertaken to confirm the change objectives were achieved and that there was no deleterious impact on product quality.

Table III: Application of Change Management System Throughout the Product Lifecycle

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Change is an inherent part of the development process and should be documented; the formality of the change management process should be consistent with the stage of pharmaceutical development.	The change management system should provide management and documentation of adjustments made to the process during technology transfer activities.	A formal change management system should be in place for commercial manufacturing. Oversight by the quality unit should provide assurance of appropriate science- and risk-based assessments.	Any changes after product discontinuation should go through an appropriate change management system.

4. Management Review of Process Performance and Product Quality (3.2.4)

Management review should provide assurance that process performance and product quality are managed over the lifecycle. Depending on the size and complexity of the company, management review can be a series of reviews at various levels of management and should include a timely and effective communication and escalation process to raise appropriate quality issues to senior levels of management for review.

- (a) The management review system should include:
 - (1) The results of regulatory inspections and findings, audits and other assessments, and commitments made to regulatory authorities
 - (2) Periodic quality reviews, that can include:
 - (i) Measures of customer satisfaction such as product quality complaints and recalls
 - (ii) Conclusions of process performance and product quality monitoring
 - (iii) The effectiveness of process and product changes including those arising from corrective action and preventive actions
 - (3) Any follow-up actions from previous management reviews
- (b) The management review system should identify appropriate actions, such as:
 - (1) Improvements to manufacturing processes and products
 - (2) Provision, training, and/or realignment of resources

(3) Capture and dissemination of knowledge

Table IV: Application of Management Review of Process Performance and Product Quality Throughout the Product Lifecycle

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Aspects of management review can be performed to ensure adequacy of the product and process design.	Aspects of management review should be performed to ensure the developed product and process can be manufactured at commercial scale.	Management review should be a structured system, as described above, and should support continual improvement.	Management review should include such items as product stability and product quality complaints.

V. CONTINUAL IMPROVEMENT OF THE PHARMACEUTICAL QUALITY SYSTEM (4)

This section describes activities that should be conducted to manage and continually improve the pharmaceutical quality system.

A. Management Review of the Pharmaceutical Quality System (4.1)

Management should have a formal process for reviewing the pharmaceutical quality system on a periodic basis. The review should include:

- (a) Measurement of achievement of pharmaceutical quality system objectives
- (b) Assessment of performance indicators that can be used to monitor the effectiveness of processes within the pharmaceutical quality system, such as:
 - (1) Complaint, deviation, CAPA and change management processes
 - (2) Feedback on outsourced activities
 - (3) Self-assessment processes including risk assessments, trending, and audits
 - (4) External assessments such as regulatory inspections and findings and customer audits

B. Monitoring of Internal and External Factors That Can Have an Impact on the Pharmaceutical Quality System (4.2)

Factors monitored by management can include:

- (a) Emerging regulations, guidance, and quality issues that can have an impact on the Pharmaceutical Quality System
- (b) Innovations that might enhance the pharmaceutical quality system
- (c) Changes in business environment and objectives

- (d) Changes in product ownership

C. Outcomes of Management Review and Monitoring (4.3)

The outcome of management review of the pharmaceutical quality system and monitoring of internal and external factors can include:

- (a) Improvements to the pharmaceutical quality system and related processes
- (b) Allocation or reallocation of resources and/or personnel training
- (c) Revisions to quality policy and quality objectives
- (d) Documentation and timely and effective communication of the results of the management review and actions, including escalation of appropriate issues to senior management

VI. GLOSSARY (5)

ICH and ISO definitions are used in ICH Q10 where they exist. For the purpose of ICH Q10, where the words “requirement”, “requirements,” or “necessary” appear in an ISO definition, they do not necessarily reflect a regulatory requirement. The source of the definition is identified in parentheses after the definition. Where no appropriate ICH or ISO definition was available, an ICH Q10 definition was developed.

Capability of a Process: Ability of a process to realize a product that will fulfill the requirements of that product. The concept of process capability can also be defined in statistical terms. (ISO 9000:2005)

Change Management: A systematic approach to proposing, evaluating, approving, implementing, and reviewing changes. (ICH Q10)

Continual Improvement: Recurring activity to increase the ability to fulfill requirements. (ISO 9000:2005)

Control Strategy: A planned set of controls, derived from current product and process understanding, that assures process performance and product quality. The controls can include parameters and attributes related to drug substance and drug product materials and components, facility and equipment operating conditions, in-process controls, finished product specifications, and the associated methods and frequency of monitoring and control. (ICH Q10)

Corrective Action: Action to eliminate the cause of a detected nonconformity or other undesirable situation. NOTE: Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. (ISO 9000:2005)

Design Space: The multidimensional combination and interaction of input variables (e.g., material attributes) and process parameters that have been demonstrated to provide assurance of quality. (ICH Q8)

Enabler: A tool or process that provides the means to achieve an objective. (ICH Q10)

Feedback/Feedforward:

Feedback: The modification or control of a process or system by its results or effects.

Feedforward: The modification or control of a process using its anticipated results or effects. (Oxford Dictionary of English by Oxford University Press, 2003)

Feedback/feedforward can be applied technically in process control strategies and conceptually in quality management. (ICH Q10)

Innovation: The introduction of new technologies or methodologies. (ICH Q10)

Knowledge Management: Systematic approach to acquiring, analyzing, storing, and disseminating information related to products, manufacturing processes, and components. (ICH Q10)

Outsourced Activities: Activities conducted by a contract acceptor under a written agreement with a contract giver. (ICH Q10)

Performance Indicators: Measurable values used to quantify quality objectives to reflect the performance of an organization, process, or system, also known as *performance metrics* in some regions. (ICH Q10)

Pharmaceutical Quality System (PQS): Management system to direct and control a pharmaceutical company with regard to quality. (ICH Q10 based upon ISO 9000:2005)

Preventive Action: Action to eliminate the cause of a potential nonconformity or other undesirable potential situation. NOTE: Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence. (ISO 9000:2005)

Product Realization: Achievement of a product with the quality attributes appropriate to meet the needs of patients, health care professionals, and regulatory authorities (including compliance with marketing authorization) and internal customers requirements. (ICH Q10)

Quality: The degree to which a set of inherent properties of a product, system, or process fulfills requirements. (ICH Q9)

Quality Manual: Document specifying the quality management system of an organization. (ISO 9000:2005)

Quality Objectives: A means to translate the quality policy and strategies into measurable activities. (ICH Q10)

Quality Planning: Part of quality management focused on setting quality objectives and specifying necessary operational processes and related resources to fulfill the quality objectives. (ISO 9000:2005)

Quality Policy: Overall intentions and direction of an organization related to quality as formally expressed by senior management. (ISO 9000:2005)

Quality Risk Management: A systematic process for the assessment, control, communication, and review of risks to the quality of the drug (medicinal) product across the product lifecycle. (ICH Q9)

Senior Management: Person(s) who direct and control a company or site at the highest levels with the authority and responsibility to mobilize resources within the company or site. (ICH Q10 based in part on ISO 9000:2005)

State of Control: A condition in which the set of controls consistently provides assurance of continued process performance and product quality. (ICH Q10)

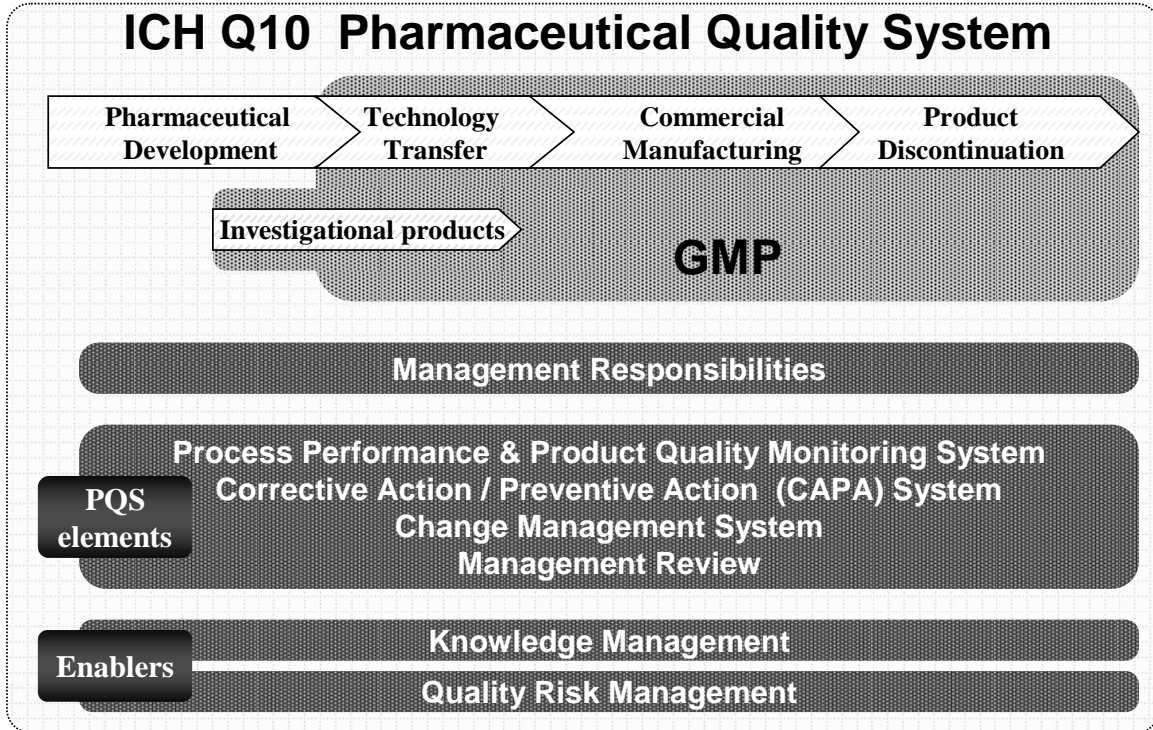
Annex I: Potential Opportunities To Enhance Science- and Risk-Based Regulatory Approaches *

*Note: This annex reflects potential opportunities to enhance regulatory approaches. The actual regulatory process will be determined by region.

Scenario	Potential Opportunity
1. Comply with GMPs	Compliance – status quo
2. Demonstrate effective pharmaceutical quality system, including effective use of quality risk management principles (e.g., ICH Q9 and ICH Q10).	Opportunity to: <ul style="list-style-type: none"> • increase use of risk-based approaches for regulatory inspections
3. Demonstrate product and process understanding, including effective use of quality risk management principles (e.g., ICH Q8 and ICH Q9).	Opportunity to: <ul style="list-style-type: none"> • facilitate science-based pharmaceutical quality assessment • enable innovative approaches to process validation • establish real-time release mechanisms
4. Demonstrate effective pharmaceutical quality system and product and process understanding, including the use of quality risk management principles (e.g., ICH Q8, ICH Q9, and ICH Q10).	Opportunity to: <ul style="list-style-type: none"> • increase use of risk-based approaches for regulatory inspections; • facilitate science-based pharmaceutical quality assessment; • optimize science- and risk-based postapproval change processes to maximize benefits from innovation and continual improvement; • enable innovative approaches to process validation; • establish real-time release mechanisms.

Annex 2

Diagram of the ICH Q10 Pharmaceutical Quality System Model



This diagram illustrates the major features of the ICH Q10 Pharmaceutical Quality System (PQS) model. The PQS covers the entire lifecycle of a product including pharmaceutical development, technology transfer, commercial manufacturing, and product discontinuation as illustrated by the upper portion of the diagram. The PQS augments regional GMPs as illustrated in the diagram. The diagram also illustrates that regional GMPs apply to the manufacture of investigational products.

The next horizontal bar illustrates the importance of management responsibilities explained in section III (2) to all stages of the product lifecycle. The following horizontal bar lists the PQS elements that serve as the major pillars under the PQS model. These elements should be applied appropriately and proportionally to each lifecycle stage, recognizing opportunities to identify areas for continual improvement.

The bottom set of horizontal bars illustrates the enablers: knowledge management and quality risk management, which are applicable throughout the lifecycle stages. These enablers support the PQS goals of achieving product realization, establishing and maintaining a state of control, and facilitating continual improvement.