

GUIDE:

Management Responsibilities and Management Review



GUIDE:

Management Responsibilities and Management Review

Disclaimer:

The ISPE APQ Guide Series provides a practical quality management framework that pharmaceutical organizations can use to assess and advance the effectiveness of Pharmaceutical Quality System elements. This Guide is solely created and owned by ISPE. It is not a regulation, standard or regulatory guideline document. ISPE cannot ensure and does not warrant that a system managed in accordance with this Guide will be acceptable to regulatory authorities. Further, this Guide does not replace the need for hiring professional engineers or technicians.

Limitation of Liability

In no event shall ISPE or any of its affiliates, or the officers, directors, employees, members, or agents of each of them, or the authors, be liable for any damages of any kind, including without limitation any special, incidental, indirect, or consequential damages, whether or not advised of the possibility of such damages, and on any theory of liability whatsoever, arising out of or in connection with the use of this information.

© Copyright ISPE 2021. All rights reserved.

All rights reserved. No part of this document may be reproduced or copied in any form or by any means – graphic, electronic, or mechanical, including photocopying, taping, or information storage and retrieval systems – without written permission of ISPE.

All trademarks used are acknowledged.

ISBN 978-1-946964-44-1

Preface

Advancing Pharmaceutical Quality (APQ) is a comprehensive program for assessing and improving an organization's quality management maturity. It is an industry-led approach that seeks to advance pharmaceutical quality beyond the submission of data for harmonized, reportable metrics. Organizations can leverage this program to ensure a continuous supply of quality medicines to patients.

The APQ program evolved from the ISPE Quality Metrics Initiative which represents extensive industry engagement, collaboration with academia and other associations, and knowledge sharing with regulatory agencies. The APQ program is harmonized with international regulatory initiatives that promote quality excellence.

APQ is built upon the ICH Q10 Pharmaceutical Quality System (PQS) model [1] that comprises management responsibilities and the following PQS elements:

- 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

The APQ program further enhances this ICH Q10 model with cultural excellence and operational excellence (continual improvement) principles. Due to the interconnectedness of management responsibilities and management review, these are addressed together for the purposes of the APQ program. The APQ Guide Series focuses on the application of the APQ framework to these four PQS elements that are based upon ICH Q10:¹

- CAPA system [2]
- Management Responsibilities and Management Review (MRR)
- Change management system
- Process performance and product quality monitoring system

The APQ Guide Series provides a practical set of tools and systematic approaches—the Assess, Aspire, Act, and Advance framework—for organizations to advance the maturity and effectiveness of these PQS elements.

This ISPE APQ Guide: MRR contains two parts. Part 1 covers the key principles of the APQ program and explains the Assess, Aspire, Act, and Advance framework. This prerequisite information is applicable to all four PQS elements. Part 2 covers the practical application of the APQ framework to the MRR principles and process. Tools and examples are provided in the appendices. Additionally, a ZIP file containing the APQ Maturity Assessment Tool (for MRR) and the APQ Benchmarking Tool is provided with this Guide at the time of purchase.

¹ The APQ Guides for the change management system and the process performance and product quality system are planned future ISPE publications.

Acknowledgements

ISPE wishes to thank all those involved in APQ who have contributed to the program and from whose work this Guide has been created.

APQ MRR Guide Team

Tisha Cromwell	Catalent Pharma Solutions	USA
Tami Frederick (APQ Advisor)	Perrigo	USA
Marci Goldfinger	Johnson & Johnson	USA
Steven Greer (Co-Lead)	ESi and Procter & Gamble	USA
Michael Griscneau (Co-Lead)	AbbVie Inc	USA
Robert Matje	RemTech LLC	USA
Lorraine McClain	Nabriva Therapeutics	USA
Jo Anne Valentino	Minaris Regenerative Medicine	USA
Veda K. Walcott	Catalent Pharma Solutions	USA
Bryan Winship	Lonza	USA

APQ Program Core Team

The following individuals contributed to the APQ program's development.

Tami Frederick (Chair)	Perrigo	USA
Erika Ballman	Perrigo	USA
Lori Chelemedos	Pac-Side LLC	USA
Andrew Denny	Bristol-Myers Squibb	USA
Joseph Famulare	Genentech, A Member of the Roche Group	USA
Betsy Fritschel	Johnson & Johnson	USA
Bethany Glyde		USA
Steven Greer	ESi and Procter & Gamble	USA
Michael Griscneau	AbbVie Inc	USA
Harry Jeffreys	Bausch Health Companies	USA
Jennifer Peszek	Pfizer	USA
Christine Smith	Eli Lilly and Company	USA
Nelson Webb	Procter & Gamble	USA
Christian Wölbeling	Körber	Germany

ISPE expresses its deep appreciation to Mairead Goetz, 2015-2019 APQ team chair, whose vision for an industry-led program to advance pharmaceutical quality gave rise to this program.

Particular thanks go to the following:

- All those who participated in the development of this Guide by reviewing or pilot testing draft material.
- Suggestions for Chapter references in THE NEW ECONOMICS by Dr. W. Edwards Deming were provided by Kelly L. Allan, Chair of the Advisory Council of The W. Edwards Deming Institute.
- Thomas Friedli, PhD, Director, Institute of Technology Management; and Marten Ritz, M.Sc., Research Associate & Head of Operational Excellence; University of St.Gallen, Switzerland for their collaboration and contributions.

The Team Leads wish to thank ISPE for the technical writing support by Nuala Calnan, PhD (BioPharm Excel, Ireland) and also to ISPE Advisor, Christopher Potter, PhD.

The Leads would like to express their grateful thanks to the individuals and companies from around the world who reviewed and provided comments during the preparation of this Guide; although they are too numerous to list here, their input is greatly appreciated.

Company affiliations are as of the final draft of the Guide.



600 N. Westshore Blvd., Suite 900, Tampa, Florida 33609 USA
Tel: +1-813-960-2105, Fax: +1-813-264-2816

www.ISPE.org

 **Documents**
Document Sharing Hub

Table of Contents

Part 1: The Advancing Pharmaceutical Quality (APQ) Program

1	Introduction to the APQ Program and Guide Series	7
1.1	Objectives	7
1.2	Scope	8
1.3	Benefits	8
1.4	About the ISPE APQ Guide Series	9
1.5	How to Use This Guide	11
2	Understanding the APQ Program	13
2.1	Link to the ICH Q10 PQS Model	13
2.2	Link to Cultural Excellence and Operational Excellence	15
3	APQ Assess, Aspire, Act, and Advance Framework	17
3.1	APQ Framework Process	18
3.2	APQ Self-Assessment Tool	19
3.3	Cross-Functional Team Approach	23
4	APQ Benchmarking	25
4.1	Benchmarking Questionnaire	25
4.2	APQ Pre-Assessment Benchmarking	27
4.3	APQ Post-Action Benchmarking	27

Part 2: Practical Application of the APQ Framework to Management Responsibilities and Management Review (APQ-MRR)

5	Introduction to APQ-MRR	29
5.1	Key Concepts Related to Effective Management Responsibilities and Management Review	30
5.2	Importance of Building and Maintaining Cultural Excellence	31
5.3	Seven APQ-MRR Elements	32
6	APQ Assess Phase	35
6.1	Assessing MRR Element 1 – Patient/Consumer Focus	36
6.2	Assessing MRR Element 2 – Management Commitment	38
6.3	Assessing MRR Element 3 – Quality Planning	46
6.4	Assessing MRR Element 4 – Internal Communication	47
6.5	Assessing MRR Element 5 – Management of Outsourced Activities and Purchased Materials	49
6.6	Assessing MRR Element 6 – Management of Change in Product Ownership	52
6.7	Assessing MRR Element 7 – Regulatory and Industry Awareness	54
7	APQ Aspire Phase	57
7.1	Evaluation of the Assigned Maturity Ratings	59
7.2	Prioritization of Targeted Improvements	59
8	APQ Act Phase	61
9	APQ Advance Phase	63

Appendices

10 Appendix 1 – APQ Program Drivers and Goals 65

10.1 What Does Advancing Pharmaceutical Quality Mean?..... 65

10.2 APQ Program Overarching Goals..... 66

11 Appendix 2 – APQ Program History: From Quality Metrics to Advancing Pharmaceutical Quality 71

12 Appendix 3 – APQ Maturity Assessment Tool for MRR 73

13 Appendix 4 – APQ Catalog of Improvement Resources and KPIs for MRR 91

14 Appendix 5 – Example APQ-MRR Assess and Aspire Report..... 97

15 Appendix 6 – Example Template for APQ-MRR Improvement Action Plan 125

16 Appendix 7 – APQ Benchmarking Tool..... 129

17 Appendix 8 – Example APQ Benchmarking Report..... 143

18 Appendix 9 – References 153

19 Appendix 10 – Glossary 155

19.1 Acronyms and Abbreviations 155

19.2 Definitions 156

1 Introduction to the APQ Program and Guide Series

The Advancing Pharmaceutical Quality (APQ) program seeks to advance the current state of pharmaceutical quality by providing a framework for assessing and enhancing the effectiveness of the Pharmaceutical Quality System (PQS).² The APQ program recognizes that the ability to advance quality management maturity lies within the industry itself; it has been developed by industry representatives for use by industry. A key driver for this program is to provide a range of sustainable, practical quality management improvement strategies, approaches, and tools for organizations.

The APQ program is built upon the ICH Q10 model [1] and enhances the PQS elements with the aspects of cultural excellence³, operational excellence (OPEX), and continual improvement.

As stated in ICH Q10:

"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." [1]

Pursuit of this desired state has always been central to ISPE's efforts to advancing the state of pharmaceutical quality within the industry. The APQ Guide Series represents the ongoing commitment towards that journey.

1.1 Objectives

The APQ program is intended to provide a comprehensive approach for assessing and improving an organization's quality management maturity in order to advance the state of quality within the organization. It is an industry-for-industry program that aims to identify good practices and good behaviors that support the continual improvement of quality management effectiveness within an organization.

The eight overarching goals of the APQ program are to:

- Integrate quality management maturity, cultural, and operational excellence principles, tools, and approaches
- Support and incentivize continual improvement
- Foster industry ownership of quality beyond compliance
- Promote effective and efficient use of resources
- Encourage self-improvement and supplier improvement
- Enable structured benchmarking, knowledge sharing, and learning among organizations
- Increase the reliability of supply for quality products
- Offer routes to delivering sustainable competitive advantage

² The Pharmaceutical Quality System (PQS) is also referred to as Quality Management System (QMS) by some organizations. For the purposes of this Guide, the term Pharmaceutical Quality System is used.

³ The terms cultural excellence and quality culture are interchangeable. For the purposes of this Guide, the term cultural excellence is used.

The APQ program intends to be relevant to individual organizations and to act as a forum for cooperation in the search for effective and practical solutions to the issues common to all organizations. The detailed discussion for the overarching goals is covered in Section 2.2 and Appendix 1.

The APQ program and APQ Guide Series are designed to incorporate the following aspects:

- Provide an industry-led program that includes a structured framework to assess and advance the effectiveness of pharmaceutical quality management, which organizations can leverage to ensure a continuous supply of high-quality medicines to their patients
- Built upon the principles of the ICH Q10 PQS [1] and further enhanced to include cultural excellence and OPEX tools, approaches, and behaviors which can support the effective management of quality
- Comprised of detailed self-assessments for quality management maturity along with self-improvement tools and KPIs focused on advancing organizational capabilities across the four core elements based on ICH Q10 PQS: CAPA system, Management Responsibilities and Management Review (MRR), change management system, process performance and product quality monitoring system
- Complement current international regulatory initiatives which promote quality excellence

1.2 Scope

The scope of the APQ Guide Series is aligned with the ICH Q10 PQS model [1] (as explained further in Section 2.1). Therefore, the practices described in the APQ Guides apply to all aspects of the PQS relevant to the manufacturing, packaging, testing, or holding of biological, chemical, advanced therapy medicinal products, combination medicinal drug products, and their associated active pharmaceutical ingredients. The principles described may also apply to medical devices, over the counter products, personal care, and cosmetics products and may be beneficially applied throughout the product lifecycle from research and development, technology transfer, commercialization, and discontinuation.

1.3 Benefits

The benefits of the APQ program are outlined below:

- Benefits for industry:
 - Access to an ICH Q10-based quality management maturity framework that can be utilized in full by an organization to understand the impact to the overall performance of the organization of their maturity assessment, Key Performance Indicator (KPI) application, and improvement actions
 - Supports sustained, continual improvement of an organization's PQS
 - Benchmarking against industry peer groups, i.e., by using the St.Gallen APQ Benchmarking Tool or full OPEX benchmarking program
 - Community of practitioners for sharing of best practices to accelerate progress
- Benefits for patients and consumers:
 - Increased reliability of supply of quality product

- Benefits for health agencies:
 - Better insight into industry's focus and current expectations regarding critical quality areas for advancing pharmaceutical quality
- Benefits for research:
 - Increased data availability for researching the impact of quality management maturity on pharmaceutical production site performance

1.4 About the ISPE APQ Guide Series

The ISPE APQ Guide Series provide a practical set of tools and systematic approaches—the Assess, Aspire, Act, and Advance framework—for organizations to advance the maturity and effectiveness of their PQS. Each APQ Guide focuses on the application of the framework to one of four elements that are based upon ICH Q10 [1]:⁴

- CAPA system [2]
- MRR
- Change management system
- Process performance and product quality monitoring system

At the core of the APQ Assess, Aspire, Act, and Advance framework is the detailed self-assessment tool to determine the current maturity level of an organization's quality system element (e.g., CAPA system). These tools integrate objective quantitative and qualitative criteria, enabling organizations to analyze the current state of quality, diagnose gaps, and identify improvement targets—**Assess and Aspire**. Using suggested continual improvement tools/resources and KPIs, organizations can then develop an Improvement Action Plan, execute it, and evaluate it for effectiveness—**Act and Advance**.

Additionally, this Guide includes a pre-assessment and post-action benchmarking questionnaire tool that organizations can use in conjunction with the APQ framework. It offers objective evidence of performance improvement to support ongoing investment of an organization's time and resources into implementing the APQ program for each quality system element. This questionnaire was developed by the Institute of Technology Management at the University of St.Gallen (Switzerland) as part of a collaboration with ISPE.

Figure 1.1 provides a high-level overview of the APQ program which comprises the APQ Assess, Aspire, Act, and Advance framework based on a foundation of cultural excellence. Figure 1.2 shows the ISPE APQ Guide Series including the application of the APQ framework to the four ICH Q10-based PQS elements, supported by additional ISPE body of knowledge and publications associated with key principles [3, 4, 5] and PQS enablers (knowledge management [6] and quality risk management).

⁴ The APQ Guides for the change management system and the process performance and product quality system are planned future ISPE publications.

Figure 1.1: Overview of the APQ Program

ISPE Advancing Pharmaceutical Quality Program

Comprehensive industry-led approach for assessing and improving the quality management maturity of Pharmaceutical Quality System elements (based upon ICH Q10)

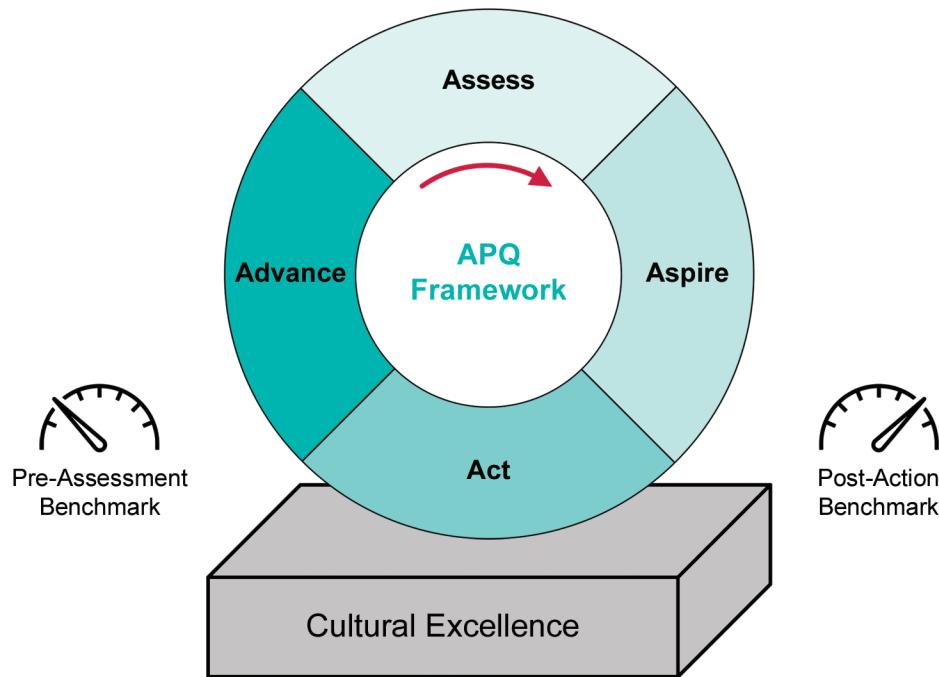
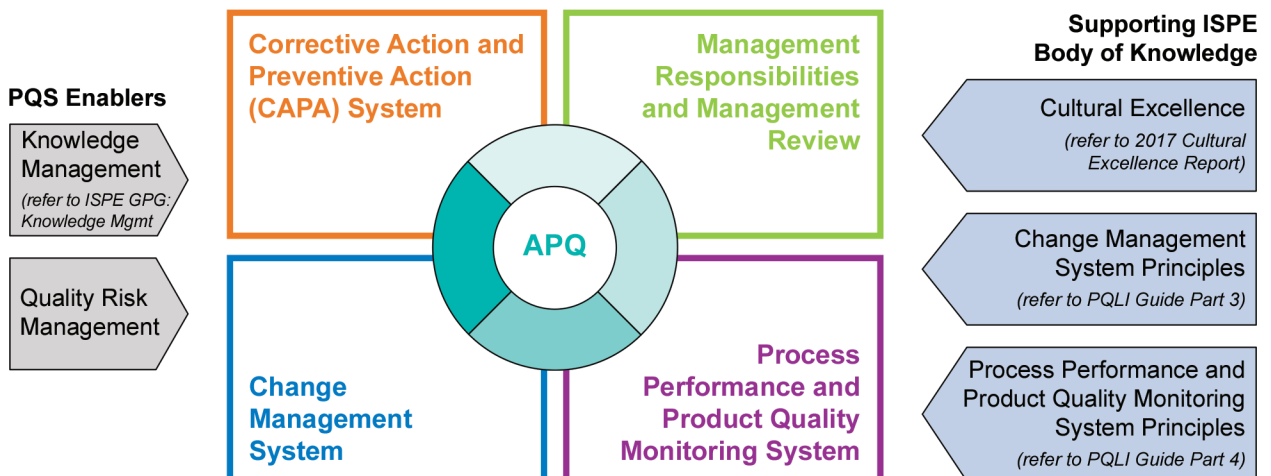


Figure 1.2: Overview of the ISPE APQ Guide Series

ISPE APQ Guide Series

Application of the APQ framework to Pharmaceutical Quality System (PQS) elements based upon ICH Q10



Note for Figure 1.2: The APQ Guides for the change management system and the process performance and product quality system are planned future ISPE publications.

1.5 How to Use This Guide

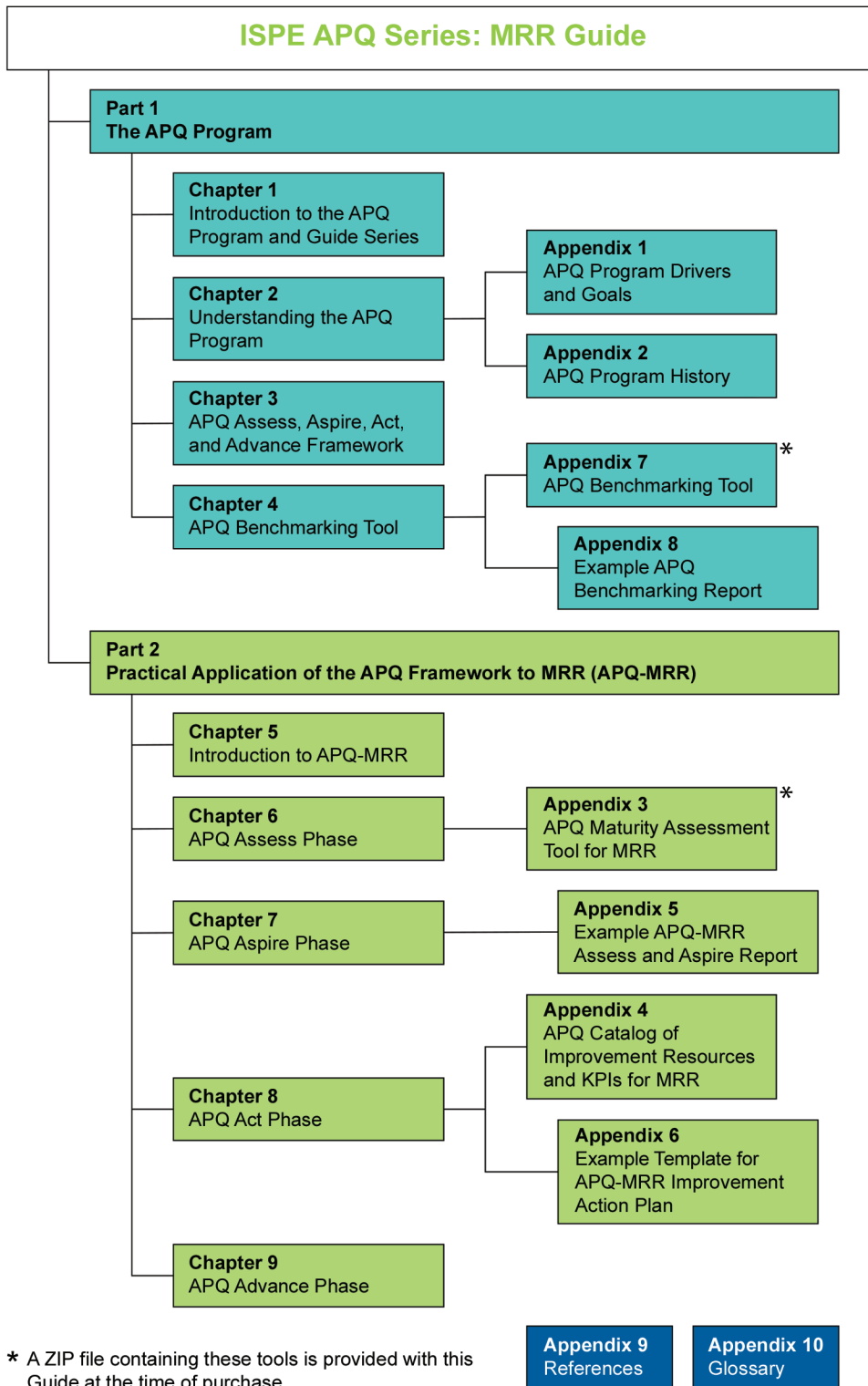
Part 1 covers the key concepts of the APQ program including the link to the ICH Q10 PQS model [1] and the link to cultural and operational excellence. It introduces the Assess, Aspire, Act, and Advance framework and explains how to perform the self-assessment. **This prerequisite information is applicable to all four PQS elements in the APQ Guide Series.** Part 1 also covers the pre-assessment and post-action benchmarking questionnaire tool.

Part 2 covers the practical application of the APQ framework to MRR (APQ-MRR). It guides readers through the four phases of the framework, explaining in detail the comprehensive self-assessment tool for diagnosing the quality management maturity of their organization's MRR principles and processes. It provides guidance on developing an APQ Improvement Action Plan, with recommended good practices and useful KPIs specific to MRR.

The appendices include a full explanation of the drivers and overarching goals of the APQ program, a summary of the program's history, and the tools and examples for practical application of the program.

Figure 1.3 provides the chapter organization of this Guide, showing the links between the body chapters and the appendices.

Figure 1.3: Guide Structure



2 Understanding the APQ Program

Robust and well-established quality systems subject to continual improvement are critical to superior performance outcomes. Organizations rely upon the effective implementation of PQS, from early development through to product approval, commercial launch, and routine supply. These aspects of a quality system are generally well considered and detailed in most pharmaceutical organizations; however, in organizations where quality management practices are less mature, there may be an emphasis on meeting compliance requirements and short-term business objectives rather than on achieving quality excellence and continual improvement. Activities that proceed well, according to plans, are usually well cared for; however, failure events or adverse situations leading to a quality defect or an interruption of supply are not always well-anticipated. The ability to predict, detect, and adapt to these events is the signature of a mature quality system.

These concepts are the basis upon which the APQ program has been designed. The APQ program is intended to be comprehensive without being complex. It has been developed to support organizations to **Assess, Aspire, Act, and Advance** the maturity and effectiveness of their quality management. The guiding principles of the APQ program are:

- Simple and practical
- Applicable across all sectors of the pharmaceutical industry
- Valuable and beneficial for industry
- Functional: Using “as is” company data, site definitions, and site procedures as much as possible
- Minimal additional work
- “By industry, for industry”
- Leveraging existing benchmarking, performance management, and OPEX methodologies and principles where relevant

The APQ program proposes that mature quality systems require the integration of excellence in quality with excellence in operations supported by excellence in organizational culture.

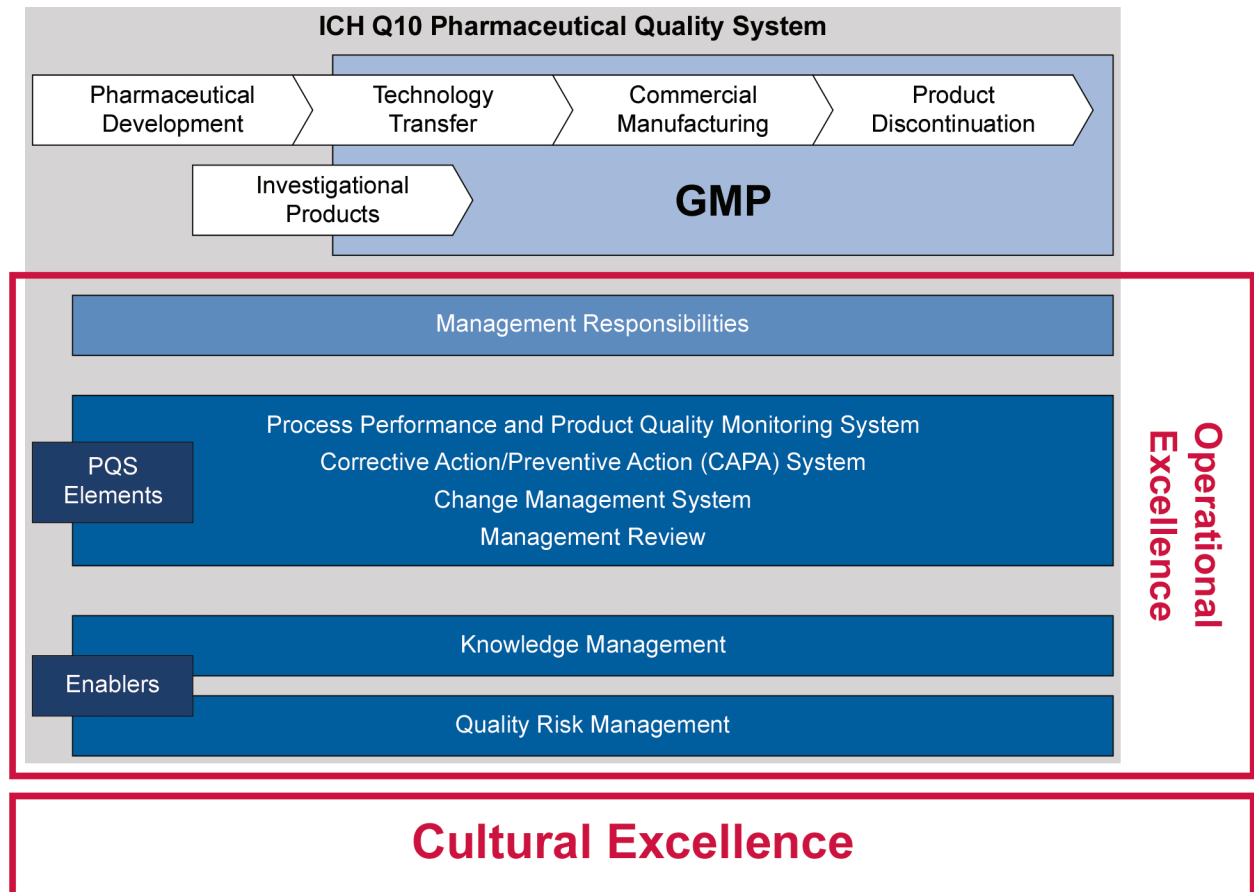
The philosophy behind the APQ program and its overarching goals is detailed in Appendix 1. It is important that readers of this Guide understand the full rationale described in this chapter and in Appendix 1 prior to the implementation of the APQ program.

For background information on how the APQ program evolved from the Quality Metrics program, see Appendix 2.

2.1 Link to the ICH Q10 PQS Model

The fundamental basis of the APQ program is the ICH Q10 PQS model [1]. Figure 2.1 shows the ICH Q10 model with APQ program enhancements (shown in red boxes) to incorporate the additional aspects of cultural excellence and OPEX.

Figure 2.1: APQ Program Link to ICH Q10 PQS Model [1]



Note: Red boxes are the APQ program enhancements to ICH Q10.

ICH Q10 states the following objectives for the implementation of the Q10 model:

- “Achieve product realization”
- “Establish and maintain a state of control”
- “Facilitate continual improvement” [1]

The concept of PQS effectiveness is raised early in the ICH Q10 guideline. Firstly, it emphasizes that the “use of knowledge management and quality risk management enable a company to implement ICH Q10 effectively and successfully.” The guideline then acknowledges that “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.” ICH Q10 recommends that “performance indicators . . . should be identified and used to monitor the effectiveness of processes within the pharmaceutical quality system.” [1]

The APQ program has been specifically developed to provide a systematic process that can be used to objectively assess and advance PQS effectiveness at a site or functional unit level through the four elements based on ICH Q10 (CAPA system, MRR, change management system, and process performance and product quality monitoring system). The APQ program includes detailed diagnostic tools, based on a 5-Level Maturity Model, for assessing and improving the effectiveness of each PQS element. A detailed description of the APQ program and how to apply it to a PQS element is provided in the next chapter (Chapter 3).

2.2 Link to Cultural Excellence and Operational Excellence

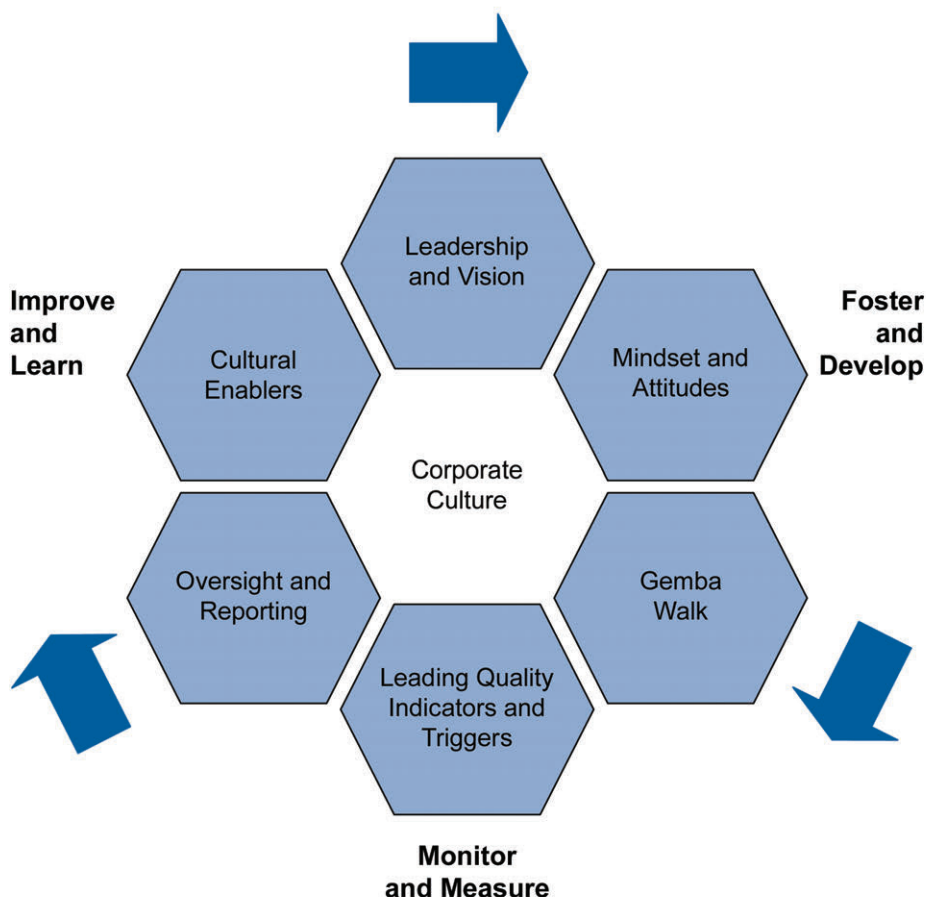
As stated earlier in this chapter, an overarching goal of the APQ program is to integrate quality, cultural, and operational excellence principles, tools, and approaches.

2.2.1 Cultural Excellence

Excellence in quality culture is essential for delivering robust and sustained quality performance, as demonstrated in the analyses from the ISPE Quality Metrics Wave 1 and Wave 2 pilot programs. [7, 8] (Background information on Quality Metrics and the relationship to APQ is covered in Appendix 2.) In Figure 2.1 (from Section 2.1), cultural excellence is depicted as the foundation stone for all other elements in the APQ program.

To address this key cultural excellence aspect, ISPE developed the six dimensions of the cultural excellence framework, as published in the 2017 ISPE Cultural Excellence Report [3] comprised of tools for assessing and improving the impact of culture on the performance outcomes for an organization. See Figure 2.2 for a diagram of the six dimensions of cultural excellence framework.

Figure 2.2: Six Dimensions of Cultural Excellence Framework [3]



There is broad alignment between the mature quality behaviors valued in the APQ assessments and the key behavioral criteria provided in the Cultural Excellence Report. For example, appropriate leadership behaviors include:

- Regular emphasis from management on quality topics and the importance of quality
- When quality issues conflict with business issues, consideration of both aspects by management before taking a decision
- Leaders regularly providing sufficient support and coaching to line workers to help them improve quality
- Leaders always modeling the desired behavior of “doing the right thing” on issues of quality

Another area of core alignment between the APQ program and the recommendations in the Cultural Excellence Report is in the design of meaningful metrics and leading quality indicators; these would include:

- Quality goals and objectives routinely established, linked, and aligned with organizational goals
- Management regularly involved in reviewing and assessing product, process, and quality system performance
- Organization’s oversight and reporting capabilities systematically applied to effectively manage external manufacturing performance within the supply chain
- Regular involvement by management of line workers in problem identification, problem solving, troubleshooting, and investigations

For those embarking on a journey to advancing pharmaceutical quality within their organization, it is recommended that the full Cultural Excellence Report (2017) [3] is read in conjunction with the ISPE APQ Guide Series.

2.2.2 Operational Excellence

Integration of the next key aspect of the APQ program relates to operational excellence (OPEX), which is defined as “a philosophy of the workplace where problem-solving, teamwork, and leadership leads to continual improvement in an organization.” [9] Continual improvement is a key goal of ICH Q10 [1] and should be considered as a critical factor for a comprehensive and sustainable OPEX initiative.

The *ISPE Good Practice Guide: Operations Management* [10] highlights that for many years the pharmaceutical industry has been successfully adopting operational approaches that come under the umbrella term “operational excellence”, including the use of improvement practices, Lean/Six Sigma techniques and tools, and the deployment and monitoring of relevant KPIs across the entire organization. The *ISPE Good Practice Guide: Operations Management* provides a useful knowledge base for promoting operational excellence within pharmaceutical operations management and is also recommended as a companion read to this Guide.

Recent research has shown, however, that quality and OPEX often exist as parallel dedicated functions in a formal pharmaceutical organizational structure, with OPEX activities managed independently of the quality unit. (Friedli, et al. [11]) Integration of these two infrastructures throughout the pharmaceutical organization is advised to more fully realize the positive impact of organization-wide improvement. The APQ Assess, Aspire, Act, and Advance framework has been carefully designed to incorporate cultural excellence behaviors and OPEX principles.

3 APQ Assess, Aspire, Act, and Advance Framework

The APQ program comprises a practical and systematic set of tools and approaches called the APQ Assess, Aspire, Act, and Advance framework that organizations can use to assess the current state of their quality management maturity at either a single site or across all sites within their organization.

The APQ Assess, Aspire, Act, and Advance framework is:

- A guided self-assessment and self-improvement process
- Comprised of four distinct but interconnected phases of Assess, Aspire, Act, and Advance
- Based on a 5-Level Maturity Model that identifies good practices and behaviors which support the advancement of quality management maturity within an organization
- Intended as an iterative, continual improvement process

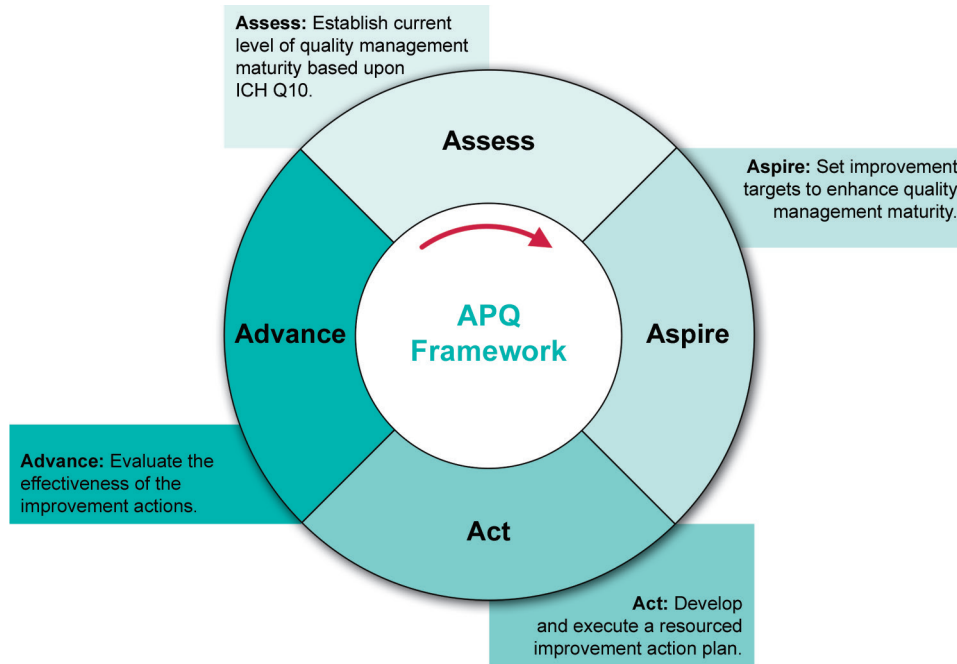
The APQ Assess, Aspire, Act, and Advance framework provides deep diagnostic tools for each of the four PQS elements based on ICH Q10 [1]:

- CAPA system
- MRR
- Change management system
- Process performance and product quality monitoring system

These self-assessment tools include detailed quantitative and qualitative criteria to evaluate the current state of quality, diagnose gaps, and identify improvement opportunities.

The APQ framework for assessment and improvement is based on the classic Plan-Do-Check-Act (PDCA) improvement cycle. It involves establishing a baseline and assessing for gaps, developing a set of systematic improvement goals, acting to advance maturity against those goals, monitoring the outcomes periodically for effectiveness, and prioritizing the next improvement opportunities. Furthermore, the program is iterative, as shown by the cycle in Figure 3.1. Ideally, continual improvement of the maturity of the PQS should remain a key focus for organizations.

Figure 3.1: APQ Assess, Aspire, Act, and Advance Framework



3.1 APQ Framework Process

This section provides a high-level overview of the four phases in the APQ framework process. Part 2 of this Guide (starting with Chapter 5) covers the practical application of the APQ framework to MRR, explaining the four phases in more detail.

1. Assess Phase

In the Assess phase, an APQ self-assessment team performs a deep evaluation of the current state of maturity of the organization's PQS with respect to the PQS elements (CAPA system, MRR, change management system, and process performance and product quality monitoring system).

The evaluation may include one or more of these PQS elements, depending on the improvement focus or business need. The APQ Benchmarking Tool described in Chapter 4 can be used to inform the prioritization of the PQS elements. For each PQS element, the detailed self-assessment is divided into a number of sub-elements to enable a deeper level of enquiry.

The APQ Maturity Assessment Tool is a deep diagnostic tool that comprises quantitative and qualitative criteria against which the PQS element maturity can be evaluated. Using the assessment tool, the team evaluates the current state of maturity, establishes objective evidence of organizational capability, and assigns an appropriate maturity rating for each sub-element. This assessment forms the basis for setting objective, measurable improvement goals.

2. Aspire Phase

In the Aspire phase, the self-assessment team analyzes the results of the assessment process to review the improvement opportunities identified and to determine where and by how much the organization aspires to improve. This analysis involves confirming the overall maturity rating for the PQS element under consideration and prioritizing the specific improvement opportunities based on current performance or business needs. An APQ Assess and Aspire Report should be prepared to summarize and present the findings from the self-assessment team. The report should be presented to management, the functional leader, and the business process owner(s) to ensure the analysis is endorsed and appropriately resourced. A formal summary report should also be presented to the executive sponsors. The output of the Aspire phase forms the basis for the Improvement Action Plan developed in the next phase.

3. Act Phase

In the Act phase, an APQ improvement team develops and executes an Improvement Action Plan for the prioritized gaps and improvements that were determined in the Assess and Aspire phases by the APQ self-assessment team. The APQ Improvement Action Plan should meet the SMART criteria—Specific, Measurable, Attainable, Relevant, and Time-bound.

To support the production of the Improvement Action Plan in the Act phase, the APQ Catalog of Improvement Resources and KPIs is a resource that action owners can leverage. It provides a listing of recommended good practices and useful KPIs specific to the PQS element undergoing the APQ framework process.

4. Advance Phase

In the Advance phase, an evaluation of the Improvement Action Plan effectiveness criteria is performed to demonstrate the achievement of the improvement goals. If the results are shown to be fully effective, reproducible, and sustainable, then the improvement team may recommend the next PQS element to be prioritized for improvement, thus commencing the next cycle of the APQ framework as an iterative process for continual improvement.

After confirmation of effectiveness has been completed in the Advance phase, a post-action benchmark may be triggered at an appropriate time point to demonstrate the impact of the improvements on the relevant company performance outcomes and KPIs.

3.2 APQ Self-Assessment Tool

3.2.1 *The 5-Level Maturity Model for Quality Management Maturity*

The APQ self-assessment tool incorporates quantitative scoring against a 5-Level Maturity Model, where **Level 1 Undefined** represents the lowest level of maturity and **Level 5 Optimized** represents the highest level of maturity.

The qualitative criteria contained within each maturity level are specific to each of the individual PQS elements, e.g., the APQ self-assessment tool for the CAPA system contains specific qualitative criteria that are distinct from the criteria for assessing maturity of the change management system.

Figure 3.2 provides descriptions for each of the five levels in the maturity model. These five levels are applicable to all PQS elements.

Figure 3.2: APQ 5-Level Maturity Model

Level 1: Undefined	Compliance Risk	Undefined	Uncontrolled	Not Monitored	No Evidence
Level 2: Defined	Partially meets ICH Q10 Requirements	Partially Defined	Not Formally Controlled	Not Formally Monitored	Person Dependent
Level 3: Managed	Fully Meets ICH Q10 Requirements	Defined Policy and Processes	Meets Requirements for Application	Process Monitoring and Controls in Place	
Level 4: Improved	Demonstrates Improved/Optimized Execution	Defined Policy and Processes	Routine Application	Routine Monitoring, Advancing Improvements	
Level 5: Optimized	World Class/ Industry Leader	Proactive	Continual Improvement	Predictive	

To determine which maturity rating should be assigned, the APQ self-assessment tool incorporates specific qualitative criteria to each of the five levels in the maturity model. The cross-functional assessment team should review evidence of maturity against the qualitative criteria and then assign the appropriate maturity rating for that PQS element.

The typical attributes of the five levels in the APQ 5-Level Maturity Model are described below:

Level 1 Undefined

An assigned maturity assessment rating of 1 indicates that the element under review is poorly or not defined, reactive, and operates on an ad hoc basis or not done at all. There are no formal controls in place and no monitoring or oversight of results/outcomes is undertaken. There is no consideration given to supply chain risk. This level of maturity represents a compliance risk.

Level 2 Defined

An assigned maturity assessment rating of 2 indicates that the element under review has been partially defined but is not formally controlled or managed by a well-defined business process. The level of understanding is limited, and the process is applied inconsistently. The operation of the process is reactive. This level of maturity is likely to arise where processes are person dependent and rely on an individual or small number of individuals to function. There is little consideration given to supply chain risk with potential for supply chain disruption. This level of maturity may be considered to partially meet ICH Q10 requirements.

Level 3 Managed

An assigned maturity assessment rating of 3 indicates that the element under review has defined policies and procedures. While this level of maturity is considered to meet the minimum ICH Q10 requirements, it may be inefficient. For example, it may have a relatively high number of CAPAs, some repetition or recurrence of events, high levels of pharmaceutical process troubleshooting, and a costly supply chain supported by high stock levels with potential for supply disruption. Improvement projects identified from CAPA processes are more likely to be focused on corrective actions. Risks to the supply chain are identified with reactive actions to resolve disruptions. Continual improvement projects are largely reactive with some traces of proactive activity. This level of maturity represents the application of the minimum acceptable standard.

Level 4 Improved

An assigned maturity assessment rating of 4 indicates that the element under review demonstrates improved execution and enhanced performance. There are well-defined policies and procedures that are routinely and effectively applied. The management review and oversight processes are routinely deployed, and improvements are identified and acted upon. The process operates on both a reactive (corrective) and proactive (preventive) basis. Risks to the supply chain are identified, understood, and proactively managed. This level of maturity fully meets ICH Q10 requirements.

Level 5 Optimized

An assigned maturity assessment rating of 5 indicates best in class. The element under review is optimized and continual improvement processes are routinely embedded in the workflow. The process is proactive, agile, and can respond quickly to the business needs. It reacts effectively with minimal resources to emerging issues and routinely operates on a proactive, preventive, and predictive basis. Oversight and review processes are optimized to drive accountability and ownership, and there is a formal responsive process for escalation. The supply chain is effective and agile with risks identified and minimized, and efficiency is optimized to its highest level. This level of maturity is best in class and is optimized to deliver maximum benefit to the business.

3.2.2 Quantitative and Qualitative Aspects

Detailed and specific qualitative criteria associated with the five maturity levels are included in the tool to guide the assessment team in accurately evaluating the current state of capabilities, competencies, and associated behaviors and to reflect those findings in the assigned maturity ratings.

Figure 3.3 illustrates the relationship between the quantitative (Maturity Rating) and qualitative (Maturity Criteria) aspects for the APQ self-assessment tool.

Figure 3.3: APQ Self-Assessment Tool – Relationship between the Maturity Rating and Maturity Criteria

Maturity Rating

Maturity Criteria

Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ No SOPs. ☐ No formal process for documenting CAPA. ☐ No monitoring or traceability oversight.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ SOP provides high-level overview and expectations (lacks details for defined responsibilities, process, and expectations). ☐ Formal process to document CAPA exists. ☐ CAPAs are monitored, however the process is not defined in an SOP.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ SOP defines process, expectations, and responsibilities across individual site or functions. ☐ Process for documenting CAPA is applied, however may have inconsistencies in execution from record to record. ☐ Monitoring process is defined in an SOP.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ SOP defines process, expectations, and responsibilities across the organization's entire network. ☐ Process for documenting CAPA is executed consistently from record to record, across the PQS (Pharmaceutical Quality System). ☐ Robust and defined monitoring ensuring successful KPI performance for the CAPA quality system.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ CAPA documentation process is periodically reviewed and proactively enhanced. ☐ Process for documenting CAPA includes full integration with PQS processes, seamless network collaboration, and proactive actions to drive continual improvement. ☐ CAPA Key Performance Indicators and Key Behavioral Indicators are engrained within the CAPA quality system. ☐ Monitoring process is proactive and assesses real time data. May include evaluating stress points and forecasting of upcoming CAPA; further granularity of CAPA for trending (category or effectiveness) is included within the documented process.

The APQ self-assessment tool provides space to contemporaneously record observations, evidence, and outcomes that may be later leveraged to develop the formal assessment report. This APQ Assess and Aspire Report, prepared in the organization's preferred format, details the findings of the assessment and the recommendations for next steps. The report should be presented to management, the functional leader, and the business process owner(s). A formal summary report should also be submitted to the executive sponsors. Each Guide in the APQ Guide Series Practical Module includes an example APQ Assess and Aspire Report.

3.3 Cross-Functional Team Approach

3.3.1 Self-Assessment Team (*Assess and Aspire*)

An APQ self-assessment team should be formed to perform the Assess and Aspire phases of the APQ framework process. The APQ program is not intended as an audit process but as an overall self-improvement process undertaken in the development of an organization. Effective self-assessment emerges from a culture of honest dialogue and critical thinking. It is best approached as a learning opportunity for a cross-functional self-assessment team made up of technical experts drawn from relevant fields such as:

- Quality Assurance
- OPEX
- Learning and development professionals
- Process owners and/or process users from independent sites in the organization

A small cross-functional team that has strong executive sponsorship is essential to ensuring an effective assessment is conducted. Potential improvements that are identified may be more difficult to implement if executive sponsorship is not secured at the outset.

This self-assessment team should actively engage with both the business process owner(s) and functional leadership of the element under assessment. This is essential to ensuring that the improvement recommendations and prioritization are agreed by all stakeholders. If this is not the case, a meeting between the sponsors, the self-assessment team, and the functional/process owner may be necessary to negotiate the next steps. The self-assessment team should have excellent interpersonal and communication skills and be committed to completing the tasks on time with a consistent approach to all criteria.

The cross-functional team approach should help to neutralize the challenges of team bias and ensure that there is an appropriate knowledge of detail within the team necessary to perform a thorough assessment. During the assessment, evidence of the following factors should be reviewed by the team to document the baseline “as found” practices, and serve as a basis for prioritizing the improvement and the post-action comparison:

- Process inputs (e.g., SOPs, process documentation/workflows, and training records)
- Execution-related documents (e.g., completed or in-process records, and related documentation)
- Demonstrated process outcomes (e.g., results, efficacy analysis, and trend analysis)
- Demonstrated behaviors such as leader standard work

It is strongly recommended that the cross-functional assessment team practice the Gemba method of “Go, Look, Ask, Coach” as part of the inquiry and assessment process. This approach ensures a full understanding of the current situation, identification of potential improvement opportunities and issues, and opportunity to provide constructive feedback to the department or function under review. The location of the Gemba walks should include observing front line activities including engagement with a cross-section of process users (e.g., attendance at CAPA meetings run by the CAPA system owner) and participation in the relevant oversight and review meetings conducted by the process and/or functional owners. For additional recommendations on how to conduct an effective Gemba activity refer to the ISPE Cultural Excellence Report [3].

Ideally, the assessment activities should be carried out by an independent self-assessment team not directly responsible for the activities under review. This team is also responsible for preparing the Aspire Report which identifies and prioritizes the improvement opportunities.

3.3.2 Improvement Team (Act and Advance)

In the Act phase, the design of the Improvement Action Plan should include engagement with key stakeholders, process owners, and process users. When the Improvement Action Plan is fully developed, ownership of the APQ framework process transitions from the self-assessment team to an APQ improvement team.

This APQ improvement team is responsible for the execution and evaluation of the APQ Improvement Action Plan during the Act and Advance phases. This team should be led by the functional owner and/or business owner of the PQS system element under review. The team should consist of the necessary cross-functional resources applicable to the improvement area(s). Oversight of the progress of this team's improvement actions should be the responsibility of the site leadership team, actively supported and sponsored by the global leadership.

4 APQ Benchmarking

The APQ program incorporates a pre-assessment and post-action benchmarking questionnaire tool developed by the St.Gallen OPEX Benchmarking team specifically for use with the APQ program.⁵ It provides standardized support to initially baseline the level of quality performance and allows organizations to prioritize which of the four ICH Q10 elements to embark upon first with the APQ framework. Used in conjunction with the APQ self-assessment and self-improvement tools, the pre- and post-benchmarking activities offer objective evidence of performance improvement to support ongoing investment of time and resources. The effectiveness and impact of the improvements from the APQ program can be evaluated and quantified, and priorities for next improvement opportunities can be derived.

4.1 Benchmarking Questionnaire

The St.Gallen APQ benchmarking questionnaire (provided in Appendix 7) can be used by organizations for either:

- Internal self-evaluation (no peer comparison possible), or
- External benchmarking against a tailored industry peer group (selected from the St.Gallen OPEX database of hundreds of pharmaceutical production sites).⁶

The benefits of opting to engage in the external benchmarking process include:

- Support from the St.Gallen team in terms of accurate data collection and completion, as part of data validation procedures applied to all datasets entering the benchmarking process
- A personalized APQ Benchmarking Report (example provided in Appendix 8) as an output of the process – this report will allow organizations to:
 - Understand individual strengths and weaknesses
 - Gain meaningful comparisons of its position as compared to a tailored peer group of comparable organizations/sites (based on the contextual factors queried in the questionnaire)

This APQ benchmarking questionnaire is a subset of the scientifically derived legacy St.Gallen OPEX benchmarking performance indicators and selected enablers that have been proven as meaningful surrogates for overall system stability and performance [9].

The APQ Benchmarking Tool is simple to use and user friendly, but still comprehensive enough to deliver a solid and balanced overview of operational performance and quality management maturity. The benchmarking tool includes:

- 13 KPIs in four dimensions (maintenance, quality, delivery, and people)
- 18 maturity questions in three categories (organization enablers, social and employee enablers, and technical and tool enablers)
- Contextual factors (such as site type and size, production technology platforms and size, and days of inventory on hand)

⁵ ISPE is in a partnership with the Institute of Technology Management at the University of St.Gallen (Switzerland) to collaborate on tools designed to advance the state of pharmaceutical quality.

⁶ For information about participating in the external benchmarking study, contact the St.Gallen OPEX Benchmarking team at benchmarking@unisg.ch. St.Gallen may collect a fee for the benchmarking service.

- High-level ICH Q10 maturity evaluation that contains questions scored on a Likert scale:
 - 71 maturity questions evaluating management responsibilities, knowledge management, CAPA system, quality risk management, process performance and product quality monitoring system, change management system, and management review
 - 8 dedicated maturity questions on Environment, Health, and Safety to complement the overall picture of maturity

This tool is intended to assist in the determination of where initial improvement efforts can be best invested.

Additionally, the St.Gallen team offers participating APQ sites that are engaged in broader business performance improvement programs an opportunity to seek synergies and upgrade the APQ Benchmarking to a full St.Gallen OPEX & QC Lab Benchmarking, which provides a more granular and comprehensive set of benchmarking results and insights.

The metrics and enablers included in the APQ Benchmarking Tool are summarized in Table 4.1.

Table 4.1: High-Level Performance Evaluation using the St.Gallen APQ Benchmarking Tool

St.Gallen APQ Benchmarking Tool			
Maintenance	Quality	Delivery	People
1. Share of Unplanned Maintenance 2. Maintenance FTE / Total FTE	3. Rejected Batches 4. Recurring Deviation 5. Quality FTE / Total FTE 6. IOOS rate (Lab) 7. Deviation Closure Time	8. Service Level – Delivery (OTIF) 9. Service Level – Supplier (OTIF) 10. Customer Complaint Rate 11. Adherence to standard lead time	12. Safety level 13. Sick leave
Enabler		Contextual Factors	
<ul style="list-style-type: none">• Organization enablers• Social and employee enablers• Technical and tool enablers		<ul style="list-style-type: none">• Site type and size• Production technology platforms and size• Days on Hand (DOH)	
ICH Q10 Maturity Assessment			
<ul style="list-style-type: none">• Management Responsibilities• Knowledge Management• CAPA System• Quality Risk Management		<ul style="list-style-type: none">• Process Performance and Product Quality Monitoring System• Change Management System• Management Review	

Refer to Appendix 7 for the APQ Benchmarking Tool and to Appendix 8 for an example APQ Benchmarking Report.

4.2 APQ Pre-Assessment Benchmarking

At the outset of the APQ framework process, it is useful to establish a baseline of current performance by formally documenting selected KPIs and organizational enablers. The goal of the pre-assessment benchmark is to set a quantitative baseline and to identify potential improvement opportunities. The APQ Benchmarking Tool can also inform the prioritization of which PQS element an organization should focus its resources to apply the deeper diagnostic APQ self-assessment tool as part of the first Assess phase. Ultimately, the results from this pre-assessment benchmark can act as an important comparator or baseline against which future advancement results can be evaluated using the post-action benchmark.

4.3 APQ Post-Action Benchmarking

At an appropriate duration after implementation of the APQ framework process (generally within an 18- to 24-month timeframe), it is recommended that post-action benchmarking is performed using the APQ Benchmarking Tool. This post-action benchmarking is intended to evaluate the impact of the improvements on the overall company performance.

The results of the post-action benchmark can be compared to the pre-assessment baseline to provide evidence of value to the business and return on investment.

As part of the iterative continual improvement process, if the overall performance goals have not yet been met, a return to the Aspire phase may be needed to identify further improvement activities or to review the effectiveness criteria. If the overall performance goals are confirmed, the next improvement opportunity may be prioritized to commence another cycle of the APQ Assess, Aspire, Act, and Advance process on any one of the four PQS elements as required.

5 Introduction to APQ-MRR

Part 2 of this Guide covers the practical application of the APQ framework to an organization's **Management Responsibilities and Management Review (MRR)** principles and processes. Due to the interconnectedness of the overall management responsibilities for the effectiveness of the organization's PQS and the various management review processes inherent within the system, MRR principles and processes are addressed together for the purposes of the APQ program.

ICH Q10 [1] provides specific guidance on management responsibilities, stating:

“Senior management has the ultimate responsibility to ensure an effective pharmaceutical quality system is in place to achieve the quality objectives...”

Regarding management review, ICH Q10 states:

“Senior management should be responsible for pharmaceutical quality system governance through management review to ensure its continuing suitability and effectiveness.”

ICH Q10 points out that the management review processes and practices should assure product quality, ensure the continuing suitability of process performance, and evaluate the effectiveness of the PQS itself. ICH Q10 holds senior management responsible for the oversight of routine periodic reviews, including the decisions and conclusions which arise.

Given the criticality of MRR to the overall implementation of the PQS, this Guide outlines how to use the APQ framework to:

- **Assess:** Evaluate the current maturity level of MRR using a Maturity Assessment Tool (Chapter 6)
- **Aspire:** Set improvement targets to enhance and improve MRR (Chapter 7)
- **Act:** Develop and execute a targeted Improvement Action Plan (Chapter 8)
- **Advance:** Evaluate the effectiveness of the improvement actions (Chapter 9)

In Chapters 6 to 9, **APQ Framework Universal Topics** are noted. These sections represent information that is universally applicable to all four PQS elements, though content may be provided in the context of MRR principles and processes for ease of understanding.

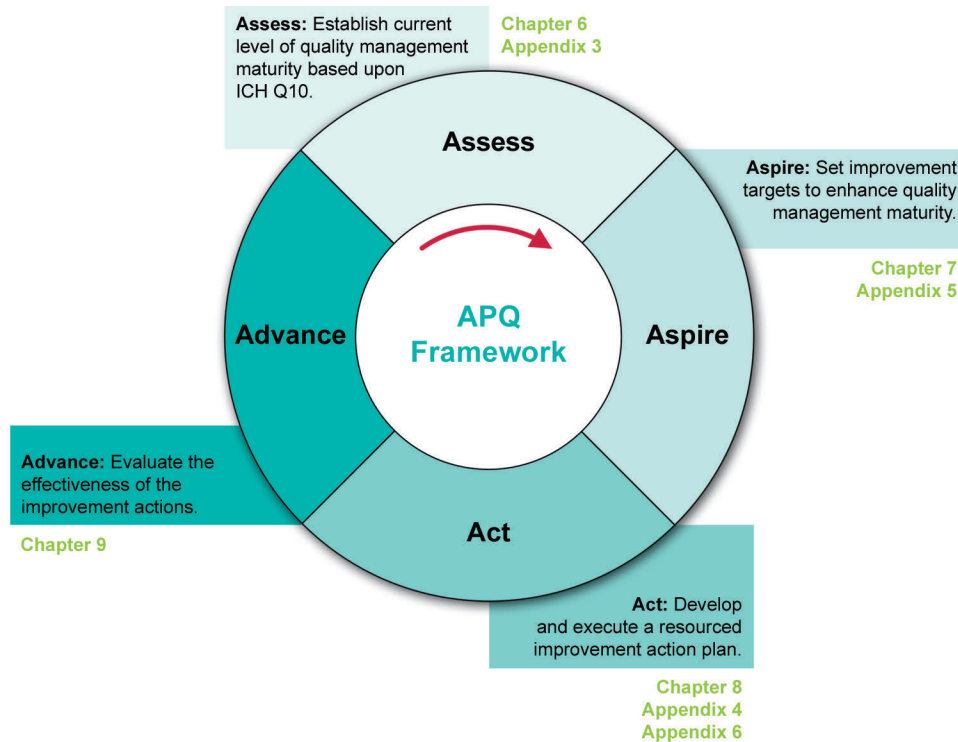
The following resources are provided in the APQ-MRR Appendices:

- APQ Maturity Assessment Tool for MRR (Appendix 3)
- APQ Catalog of Improvement Resources and KPIs for MRR (Appendix 4)
- Case studies:
 - Example APQ-MRR Assess and Aspire Report (Appendix 5)
 - Example Template for APQ-MRR Improvement Action Plan (Appendix 6)

Note: The information presented in Part 2 of this Guide builds on the prerequisite explanation of the APQ framework in Chapter 3.

Figure 5.1 provides a roadmap of the application of the APQ framework to MRR, with chapter references for each phase of the framework.

Figure 5.1: Practical Application of the APQ Framework to MRR – Roadmap



5.1 Key Concepts Related to Effective Management Responsibilities and Management Review

ICH Q10 [1] sets a clear expectation regarding the role of strong leadership in terms of demonstrating and communicating “*strong and visible support for the pharmaceutical quality system*” with an ongoing commitment to quality across the organization, product lifecycle, and complex supply chains involved in the delivery of safe and effective medicines to the patient. This commitment to quality includes the proactive review and oversight of the performance of the PQS.

ICH Q10 states:

“Leadership is essential to establish and maintain a company-wide commitment to quality and for the performance of the pharmaceutical quality system.” [1]

In terms of roles and responsibilities, ICH Q10 defines the term *senior management* as follows:

“Person(s) who direct and control a company or site at the highest levels with the authority and responsibility to mobilise resources within the company or site.”

This *senior management* group has the ultimate responsibility to ensure that the PQS is effective. ICH Q10 emphasizes that an effective PQS can “*enhance the quality and availability of medicines around the world in the interest of public health.*” These dual objectives of high quality and continuity of supply should be central to the MRR principles and processes. There is also a growing recognition that two further aspects highlighted in ICH Q10 are crucial to any evaluation of effectiveness, namely innovation and continual improvement.

“Implementation of ICH Q10 throughout the product lifecycle should facilitate innovation and continual improvement and strengthen the link between pharmaceutical development and manufacturing activities.” (ICH Q10 [1])

Innovation is defined as the *“introduction of new technologies or methodologies”* [1] and continual improvement is defined as an ongoing or *“recurring activity to increase the ability to fulfill requirements”* [1].

The APQ program offers a structured framework to advance quality management maturity beyond compliance by enhancing PQS effectiveness, enabling continual improvement and encouraging innovation. Companies that advance quality management maturity routinely leverage technology and knowledge management and focus on key activities such as risk management and continual improvement. These companies focus on predicting and preventing manufacturing problems, enabling the company to act promptly and continually improve product quality while also improving overall business performance. The FDA Drug Shortages Task Force report (2019) [12] states:

“As companies move from a focus on compliance with CGMPs to institutionalizing continual process and system improvement efforts, they begin to advance in quality management maturity.”

The key concepts for effective MRR principles and processes are closely aligned with the overarching goals of the APQ program (see Section 1.1 and Appendix 1), which include but are not limited to:

- Fostering senior management ownership of quality beyond compliance
- Integrating quality management maturity with cultural and OPEX principles
- Supporting and incentivizing continual improvement

Implementing these concepts not only increases the reliability of supply for quality products but also offers routes to delivering a sustainable, competitive advantage for the organization. The APQ program provides a systematic and proactive approach to the identification and prioritization of improvement opportunities. The inclusion of the pre-assessment and post-action benchmarking tool enables objective evidence of performance improvement for the business.

Ultimately, a mature PQS is a direct reflection of the vision of senior management and the culture of the organization. The next section of this Guide addresses the importance of building and sustaining a culture of excellence within the organization in delivering value for the patients and the business.

5.2 Importance of Building and Maintaining Cultural Excellence

Instilling a strong quality culture is essential for delivering robust and sustained quality performance. For this reason, cultural excellence is depicted as the foundation stone for all other elements in the APQ program (see Section 2.1). The FDA Drug Shortages Task Force report [12] acknowledges the critical role of culture, stating:

“A strong quality culture across the organization demonstrates that product quality and its impact on the patient drives corporate strategy and decisions. For example, this might include ensuring that employees understand patient impact, can escalate potential quality issues effectively, and are rewarded based on quality outcomes. Senior management’s commitment to quality can play a central role in driving quality culture by supporting staff development programs (e.g., mentoring, training, staff development plans, and in shop-floor operations.)”

The APQ **Assess, Aspire, Act, and Advance Framework** has been carefully designed to incorporate cultural excellence behaviors and OPEX principles. There is broad alignment between the mature quality behaviors contained in the APQ assessments and the key behavioral criteria provided in the ISPE Cultural Excellence report [3]:

- From the perspective of management responsibilities, appropriate leadership behaviors highlighted include:
 - *"We regularly hear from management an emphasis on quality topics and the importance of quality."*
 - *"When we have quality issues in conflict with business issues, both aspects are always considered by management before taking a decision."*
 - *Leaders regularly provide sufficient support and coaching to line workers to help them improve quality."*
 - *Leaders always model the desired behavior of 'doing the right thing' on issues of quality."*
- From the perspective of management review, practical OPEX led approaches for designing meaningful metrics and leading quality indicators include:
 - *"Quality goals and objectives are routinely established, linked, and aligned with organizational goals."*
 - *Management is regularly involved in reviewing and assessing product, process and quality system performance." Management takes action on the outcomes."*
 - *"The company's oversight and reporting capabilities are systematically applied to effectively manage external manufacturing performance within the supply chain."*
 - *Management regularly involves line workers in problem identification, problem solving, troubleshooting and investigations."*

Leadership owns creating and clearly communicating to everyone in the organization a vision that fosters a culture of excellence. Leaders will benefit from a deeper understanding of the underpinning philosophy and rationale behind the eight overarching goals of the APQ Program to ensure the correction application of the **Assess, Aspire, Act, and Advance Framework**. Further details of these goals can be found in Appendix 1.

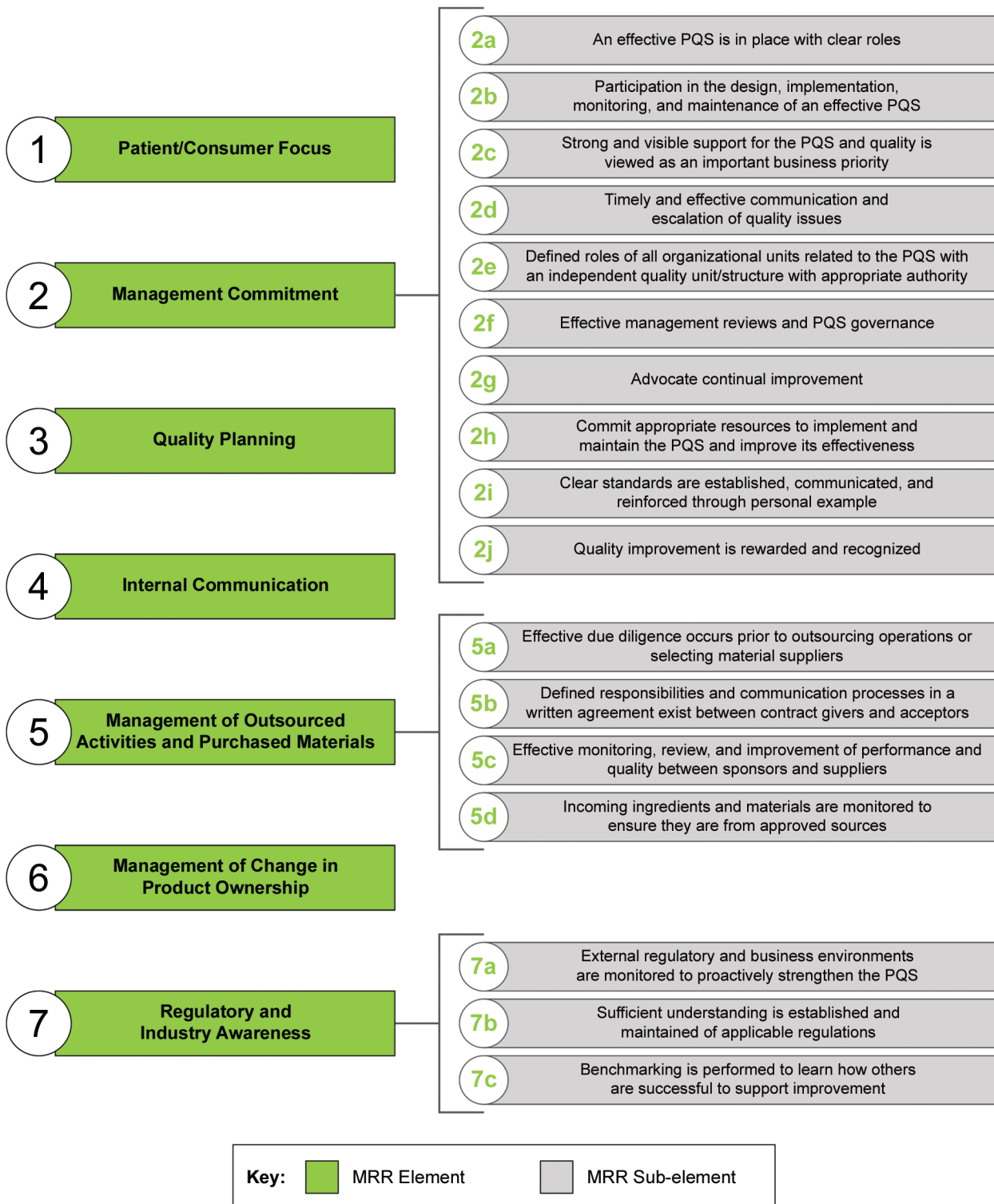
5.3 Seven APQ-MRR Elements

For the APQ-MRR program, the principles and process are categorized into seven distinct MRR elements as shown in Figure 5.2. These MRR elements are consolidated and informed by the aspects of management responsibilities highlighted in ICH Q10 [1] and augmented by industry insights to embrace other key aspects of management and organizational capability.

The APQ program emphasizes that a mature approach to quality management starts with a patient/consumer focus. For this reason the evaluation of this MRR element has been placed first in the APQ-MRR assessment tool. This is aligned with the FDA Drug Shortages Task Force report (2019) [12].⁷ MRR Elements 2 through 6 are directly related to the management responsibilities outlined in ICH Q10 [12] and may be familiar to many. To close out the seven MRR elements, and perhaps less common, is the recommendation to implement practices that build and maintain awareness of external changes in the global regulatory and industry landscape. MRR Element 7, Regulatory and Industry Awareness has been included to encourage external engagement and continual improvement.

⁷ "Quality management maturity starts with a foundational QMS that conforms to CGMPs and builds in a performance and patient focus that utilizes technology, statistical process control, and planning activities such as risk-management and continuous improvement plans." FDA Drug Shortages Task Force report (2019) [12]

Figure 5.2: APQ-MRR Elements and Sub-elements



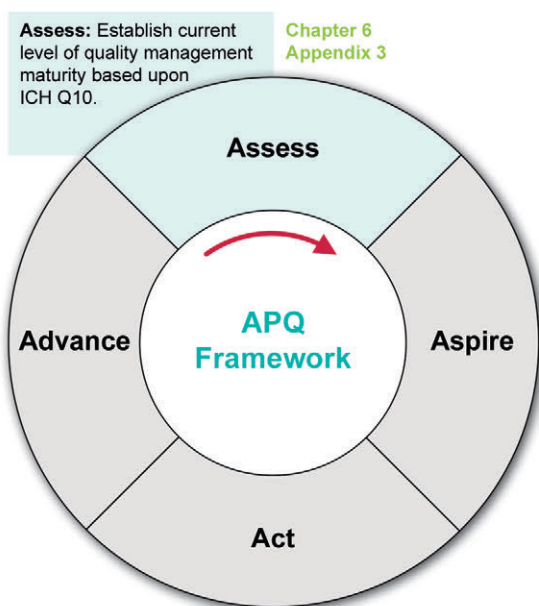
Detailed qualitative evaluation criteria for each of these seven MRR Elements (including the seventeen sub-elements) are provided in the APQ-MRR Maturity Assessment Tool, discussed in detail in Chapter 6 and provided in Appendix 3.

6 APQ Assess Phase

In the APQ Assess phase (see Figure 6.1), the cross-functional self-assessment team performs an evaluation of the current maturity state of the organization's PQS with respect to the MRR principles and processes. Refer to Section 3.3 (Cross-Functional Team Approach) for more details on the purpose and function of the assessment team. Using the APQ Maturity Assessment Tool, the team evaluates the current state of maturity, establishes objective evidence of organizational capability, and assigns an appropriate maturity rating for each MRR element. This chapter covers the self-assessment tool in depth and explains the rationale for the assessment criteria. The full APQ Maturity Assessment Tool for MRR is provided in Appendix 3.

Note: The information presented in this chapter builds on the description of the APQ framework in Chapter 3.

Figure 6.1: APQ-MRR Guide – Assess Phase



APQ FRAMEWORK UNIVERSAL TOPIC

The APQ Assess phase is a guided process using objective quantitative and qualitative criteria to assess business process capabilities and performance, leadership and workforce competencies, and associated behaviors of the selected PQS element (e.g., MRR, CAPA, etc.). The self-assessment process enables a proactive and transparent review of current practices and outcomes in order to determine the current level of quality management maturity.

For each MRR element assessed using the APQ Maturity Assessment Tool, the self-assessment team should observe, review, and provide demonstrated evidence of current policy and practice against specific criteria set out across the 5-Level Maturity Model. This includes seeking evidence of quality system aspects such as relevant procedures, checklists, and forms, as well as observing the behaviors of senior management and the impact of those behaviors on the organization.

Most of the criteria within a given maturity level should be met in full, as determined by the self-assessment team, in order to assign that maturity rating. The maturity ratings can then be actioned individually or grouped as a weighted rating for the PQS element under review. Organizations are encouraged to prioritize elements for improvement, and this Guide provides the option to assign an overall maturity rating to each MRR element, if helpful.

6.1 Assessing MRR Element 1 – Patient/Consumer Focus

A distinguishing feature of an organization that aspires towards a culture of quality excellence is that it routinely positions patient/consumer quality and safety as a primary focus. A mature and effective PQS integrates and promotes principles that ensure a patient/consumer focus is maintained and monitored.

While the phrase *patient focus* may not be explicitly found in regulatory requirements, patient safety is implicit in both the intent and the letter of the regulations. EU GMP Volume 4, Chapter 1: Pharmaceutical Quality System [11] states:

“The holder of a Manufacturing Authorisation must manufacture medicinal products so as to ensure that they are fit for their intended use, comply with the requirements of the Marketing Authorisation or Clinical Trial Authorisation, as appropriate and do not place patients at risk due to inadequate safety, quality or efficacy.”

When patient/consumer focus is at the center of the business, it is evident throughout the organization in terms of priorities and risk-based decision making. In organizations where there is a true passion for the patient/consumer, it can be both inspiring and contagious. The value of this passion can be realized across multiple fronts in terms of organizational performance outcomes. The voice of the patient is often evident in employee meetings (such as town halls) and external community and social engagements. Patient/consumer focus is systematically built into the organization’s innovation strategy. Where possible, opportunities for employees to directly interface with patients/consumers are encouraged to drive greater understanding of their needs and to strengthen quality improvement activities. For suppliers without direct patient interface, such as Contract Manufacturing Organizations (CMOs) or critical material suppliers who may have greater focus on their customer’s needs, alternative approaches can be utilized to establish a clear line of sight to the end users and to create a patient/consumer centric culture. It is important that everyone in the organization, including front line personnel, understand how their roles are connected to patient safety, quality, and efficacy. Therefore, involving these personnel in patient/consumer feedback is an important aspect in prioritizing improvements.

When a lack of patient/consumer focus in either the business or Quality objectives is evident throughout an organization, priorities are often driven by primarily internal factors, such as cost or volume drivers, and the PQS is often found to be less mature in terms of both its effectiveness and efficiency.

The detailed evaluation criteria for the Patient/Consumer Focus MRR element are provided in Table 6.1.

Table 6.1: Assessment Criteria for Patient/Consumer Focus

MRR Element 1: Patient/Consumer Focus			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Little or no evidence of patient/consumer focus in the business or in the Quality objectives.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ There is some evidence of patient/consumer focus (e.g., patient/consumer feedback is used to set improvement priorities), but it may be superficial and priorities are primarily internally based.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ There is evidence of patient focus throughout the organization (e.g., operators understand how their roles are connected to patient safety and quality). ☐ Patient/consumer feedback, where possible, is taken into account when prioritizing improvements.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ Patient/consumer focus is very evident throughout the organization, and the impact on the patient/consumer is evaluated and prioritized. ☐ Voice of the patient is very evident in employee meetings (such as town halls) and built into the innovation strategy. ☐ For suppliers without direct patient interface, alternative approaches are utilized to create a patient centric culture. ☐ Employees interface directly with patients/consumers, where possible, to enhance empathy, drive greater understanding of their needs, and strengthen quality improvement activities.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ Patient/consumer focus is at the center of the business and is evident throughout the organization at all levels, from the shop floor through senior management. ☐ There is clear evidence of a patient/consumer focus in enhanced attention to detail, priority setting, decision making, and measurement of performance outcomes. ☐ The passion for the patient/consumer is inspiring and contagious, valued across levels.

6.2 Assessing MRR Element 2 – Management Commitment

Regarding management commitment, ICH Q10 [1] states:

“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.”

There is a direct linkage between the level of cultural excellence and the level of management commitment and engagement demonstrated by senior management, both strategically and operationally, on a daily basis. The APQ Assess evaluation for this MRR element includes a range of sub-elements to determine senior management's willingness to actively sponsor and champion quality excellence. These sub-elements are based on ICH Q10 [1] and described as follows:

- a. Responsibility to ensure an effective PQS is in place to achieve Quality objectives
- b. Participating in the design, implementation, monitoring, and maintenance of an effective PQS
- c. Demonstrating strong and visible support for the PQS and ensuring its implementation throughout their organization; demonstrating by their own actions and behaviors that the organization is committed to quality as an important business priority
- d. Ensuring a timely and effective communication and escalation process exists to raise quality issues, cross-functionally, to the appropriate levels of management
- e. Defining individual and collective roles, responsibilities, authorities, and interrelationships of cross-functional organizational units related to the PQS; ensuring these interactions are communicated and understood at all levels of the organization
- f. Conducting proactive management reviews of process performance and product quality and of the PQS to ensure its continuing suitability and effectiveness; routinely assessing the conclusions of these periodic reviews; cascading any material findings and opportunities for improvement to line management for resolution and follow-up
- g. Advocating and prioritizing continual improvement
- h. Committing appropriate resources to implement and maintain the PQS and to continually improve its effectiveness
- i. Setting clear standards (e.g., establishing leader standard work) for activities; ensuring that these standards are communicated to all and reinforced through their own personal example, with defined responsibilities, clear accountability, and measurable leading behavioral indicators
- j. Actively sponsor systems to reward and recognize employee behaviors that contribute to improvements either in the Quality systems or in quality performance outcomes, thus demonstrating their commitment to the realization of PQS effectiveness

The Management Commitment MRR element of the APQ Maturity Assessment Tool represents the core of effective MRR processes and evaluates a wide range of key criteria across these ten distinct sub-elements. The detailed evaluation criteria for the Management Commitment MRR element are provided in Table 6.2.

Table 6.2: Assessment Criteria for Management Commitment

MRR Element 2: Management Commitment			
Sub-element 2a: An effective PQS is in place with clear roles			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Senior management has not defined Quality objectives, roles, responsibilities, applicable authorities, nor proactively communicated these to the company.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Senior management has begun to establish a Quality policy, Quality objectives, Quality plan, and the mechanisms to define the roles and communication channels. ☐ Training programs are GMP compliance-focused, “read and understand” format with little or no evaluation of training effectiveness.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ Senior management has implemented a Quality policy, Quality objectives (including measurable metrics), and Quality plan. ☐ Senior management has assigned responsibility and authority for the elements of the Quality system. ☐ There is linkage between Quality objectives and the business strategy. ☐ Structured role-specific training programs are in place that include a level of basic assessment and evaluation of knowledge transfer.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ Employees in the organization understand the Quality policy and objectives and have personal deliverables and development activities that are linked to Quality objectives and plans. ☐ There is a clear linkage between the business strategy and the documented Quality objectives and plan. This is used to ensure resources are appropriately applied to specific products, processes, etc. ☐ Senior management has a systematic process for periodically reviewing the Quality policy for continuing effectiveness and improvement. ☐ An emphasis is placed on individual development through well-resourced and documented learning and development programs. Opportunities to practice and master new skills within team environments, including feedback, enables assessment and evaluation of knowledge transfer effectiveness.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ PQS improvement and policy development are at the heart of the long-term business strategy development processes within the organization. ☐ The entire organization, led by senior management’s example, proactively utilizes planning objectives, specific metrics, resource management (human, financial, materials, facilities, and equipment), and CAPAs in conjunction with tools, techniques, and proactive communication to consistently identify and reduce safety, regulatory, quality, reliability, and business risks. ☐ All personnel continually strive to operate as a learning organization. Reflection and improvement processes are embedded within the daily workflows, and individuals take personal responsibility for their own and their team’s ongoing competency development to maintain and retain best-in-class talent.
Sub-element 2b: Participation in the design, implementation, monitoring, and maintenance of an effective PQS			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ PQS is not considered a priority by management, resulting in an incomplete and ineffective system.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Senior management has delegated responsibility to establish and improve/ sustain the PQS. ☐ Focus is on compliance rather than providing a framework for adding value to the organization.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ An effective PQS is in place, and Quality objectives are established. ☐ Senior management approves PQS policies and ensures that these are communicated, understood, and implemented throughout the organization. ☐ System health checks of major Quality systems are performed. ☐ Quality performance monitoring is largely done by periodic review of lagging metrics and is the responsibility of the Quality unit.

MRR Element 2: Management Commitment (continued)			
Sub-element 2b: Participation in the design, implementation, monitoring, and maintenance of an effective PQS (continued)			
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	<ul style="list-style-type: none"> ☐ Cross-functional management routinely communicates the importance of an effective PQS to meet customer and regulatory requirements across all levels of the organization. ☐ Cross-functional management demonstrates ownership of the PQS, directly supports its design and monitoring, and is available to support implementation as needed. ☐ System health checks, internal audits, and systematic reviews of the effectiveness and performance of Quality systems are routinely performed and used to drive continual improvement. Results of these checks are visible to all employees who are actively engaged in the improvement programs. ☐ Investment in terms of skills development, time, and capital in the ongoing monitoring, maintenance, and development of the PQS is central to business planning activities.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	<ul style="list-style-type: none"> ☐ Senior management is promoting and leading the drive for shared best practices within industry, and engaged employees actively implement these practices within the organization. ☐ All employees demonstrate ownership and communicate the importance of an effective and efficient PQS to exceed customer and regulatory requirements across all levels of the organization. ☐ The data and knowledge captured within the PQS business processes are valued, accessible, and utilized as a key source of competitive advantage for the organization.
Sub-element 2c: Strong and visible support for the PQS and quality is viewed as an important business priority			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	<ul style="list-style-type: none"> ☐ Discussions about Quality and Quality results rarely occur. ☐ Senior management interaction with employees on Quality is highly dependent on the leader – very low visibility that leadership places value on Quality unless addressing a problem.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	<ul style="list-style-type: none"> ☐ Meetings and reviews occur periodically to discuss Quality but are typically focused on reactively resolving issues. ☐ Senior management interaction with employees regarding Quality is unstructured and dependent on the leader.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	<ul style="list-style-type: none"> ☐ Regular meetings and reviews occur to discuss Quality plans and results with actions being taken resulting from the reviews. These reviews are largely owned by the Quality unit. ☐ A Gemba system (or similar) is in place to foster leadership interaction on Quality but may operate on a relatively infrequent basis, e.g., a monthly or biweekly basis.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	<ul style="list-style-type: none"> ☐ Leaders interact effectively and frequently across all levels of the organization and positively influence employee mindset and attitudes about the importance of Quality. ☐ Effective Gemba and tiered accountability processes (e.g., visual factory, status boards, etc.) exist in front line operations, supporting functions, and administrative areas. ☐ Reward and recognition programs are used by leaders and peers to recognize “critical to quality” behaviors and positively reinforce demonstration of the company values.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	<ul style="list-style-type: none"> ☐ The high value placed on Quality is demonstrated by everyone across the organization, consistently and in a very visible manner – everyone knows that Quality is a top priority. ☐ Best-in-class Gemba processes exist that foster strong coaching and collaborative efforts between leaders and all employees on continual improvement. ☐ All employees are engaged and empowered to take accountability and ownership for quality performance. Individual development plans are designed to develop the skills and competencies necessary to enable employees to deliver their best work in support of the strategic priorities.

MRR Element 2: Management Commitment (continued)			
Sub-element 2d: Timely and effective communication and escalation of quality issues			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ No formal mechanisms by which communications are cascaded.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Pockets of the organization have effective communication but is highly dependent on individual leaders. ☐ Overall, leaders recognize the need for a more structured approach but have not yet taken action on the observation.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ Policies and procedures formalize regulatory requirements. ☐ Adherence to requirements, as demonstrated through management reviews of the Quality system, including clear and appropriate escalation of Quality issues. ☐ A formal senior management team (i.e., Quality council) structure with regular meetings promotes the cascading and escalation of Quality risks and issues. This review process is largely focused on reactive responses to issues that have already been raised.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ Clear escalation pathways exist between all levels of the organization from the front line to the senior management (e.g., shift huddles, tiered accountability meetings, etc.). Issues are escalated up and decisions are communicated back down in a timely manner. ☐ Communication expectations are formally monitored for both implementation and effectiveness. ☐ Systematic communication processes are in place to promote the strategic objectives and vision, enable greater alignment of efforts, and share best practices across the organization, e.g., town halls, company intranet, Communities of Practice (CoPs).
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ Internal communications include external perspectives from regulators and patients as well as internal perspectives from employees and "voice of process". ☐ Organizational knowledge (e.g., best practices/lessons learned) are formally captured and pulled through the organization as available assets. ☐ Forums exist for cross-functional teams to share learning, challenges, and successes. ☐ All employees are actively involved in the proactive communication of risks, trends, opportunities, and challenges, etc. to predict and prevent Quality issues.
Sub-element 2e: Defined roles of all organizational units related to the PQS with an independent quality unit/structure with appropriate authority			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Roles and responsibilities for the Quality unit are not clear leading to ineffective execution and lack of accountability. ☐ The Quality unit is not empowered with sufficient authority to fulfill its role.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Roles and responsibilities for the Quality unit are somewhat clear within the organization but gaps exist between functions/locations leading to risk and/or ineffective execution. ☐ The Quality unit is somewhat independent but not sufficiently empowered to fulfill its role.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ Roles and responsibilities are clear both within and between organizations with minimal risk, but some efficiency gaps exist. ☐ Job descriptions are clear about the Quality unit responsibilities. ☐ The overarching organizational structure is clearly defined and understood, with the Quality unit independent and empowered to fulfill its role. ☐ Quality Assurance and Quality Control independence is documented.

MRR Element 2: Management Commitment (continued)			
Sub-element 2e: Defined roles of all organizational units related to the PQS with an independent quality unit/structure with appropriate authority (continued)			
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> Defined policy and processes Routine application Routine monitoring, advancing improvements 	☐ Roles and responsibilities are clear within and between organizations with no risk; some remaining efficiency opportunities exist. ☐ High levels of cross-functional collaboration exist between the PQS process owners within the Quality unit and the PQS process users throughout the organization in support of continual improvement of Quality. ☐ The Quality unit is independent, empowered, and seen as a significant stakeholder in all decision making within the organization. ☐ There is high ownership of Quality throughout the technical side of the organization, and the Quality unit partners with the commercial organization to align goals and drive business growth.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> Proactive Continual improvement Predictive 	☐ Roles and responsibilities are optimized, leading to a highly effective and efficient organization. ☐ The Quality unit is independent and empowered and seen as a full business partner driving value across both technical and commercial aspects of the organization. ☐ The responsibility for Quality is visibly owned by all.
Sub-element 2f: Effective management reviews and PQS governance			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> Undefined Uncontrolled Not monitored No evidence 	☐ Senior management has begun to establish a formal management review process but one is not in place or effective.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> Partially defined Not formally controlled Not formally monitored Person dependent 	☐ Requirements exist and are documented for management review of the Quality system, and a management representative has been assigned but the program is not effective.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> Defined policy and processes Meets requirements for application Process monitoring and controls in place 	☐ An effective management review process is established with guidance from policy, SOP, and charters. ☐ Information flows appropriately from plants/CMOs up to leadership through a tiered approach. ☐ The linkages between multiple Quality system elements are evident in management review (e.g., CAPA, deviations, internal audits, product complaints, etc.). ☐ Conclusions from periodic reviews of process performance, product quality, and the health of Quality systems are integrated into reviews. ☐ The management review process may have some aspects that are not as effective or efficient in execution or in delivering the desired results.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> Defined policy and processes Routine application Routine monitoring, advancing improvements 	☐ Quality system metrics and PQS effectiveness measures (represented by KPIs) include proactive/predictive measures and are routinely reviewed by senior management, driving appropriate and timely actions. ☐ Senior management (both within and exterior to the Quality unit) are visibly and actively involved in the oversight and support of Quality system effectiveness to ensure successful fulfillment of supply chain commitments. ☐ Product level reviews are routinely conducted using up-to-date continued/ ongoing process verification data to confirm processes remain in a state of control.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> Proactive Continual improvement Predictive 	☐ Highly effective and efficient integrated system for capturing, reviewing, and reporting on Quality KPIs, issues, opportunities, and requests for help from plants/CMOs to leadership. ☐ Leaders utilize the information to act in a proactive/predictive manner to address potential risks/issues and leverage opportunities to improve Quality and Quality system effectiveness. ☐ Visibility and ownership for performance outcomes and continual improvement is fully established throughout the organization. Leaders act as mentors and coaches.

MRR Element 2: Management Commitment (continued)			
Sub-element 2g: Advocate continual improvement			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Work processes are improved when necessary (e.g., CAPA, significant business loss, etc.).
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Improvements are made to work processes but there is not a consistent focus on improvement. ☐ Quality plan or statement of commitment is established to support improvement.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ A Quality policy states the importance of continual improvement of the PQS. ☐ Basic continual improvement methodology (Kaizen, Gemba, etc.) are used occasionally to understand and take action upon opportunities for continual improvement. ☐ Mechanisms and culture are in place to encourage elevation of Quality issues, but gaps exist in terms of implementation.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ The Quality plan outlines how to utilize the company's continual improvement program to enhance the Quality system and drive results improvement. ☐ Continual improvement, OPEX/Lean Six Sigma methodologies are routinely used as a means of proactively looking for and acting upon improvements in work processes. ☐ Continual improvement is ingrained in all business processes across the organization/site. ☐ Employees are empowered to elevate issues and suggest improvement ideas, etc. A systematic process for review and prioritization of these suggestions exists, and front line teams are involved in solution building. ☐ Quality "near miss" events are analyzed as a learning opportunity and utilized to drive improvement.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ There is high visibility and ownership of continual improvement, and the outcomes and results are made public. ☐ Reward and recognition program is highly developed and used frequently with peer-to-peer recognition; leader rewards linked to the organization's core values are awarded to reinforce the "critical to quality" behaviors while reinforcing full engagement of the organization. ☐ Continual improvement occurs across the supply chain, driving value for stakeholders beyond the site. ☐ Third-party partnerships (critical material suppliers, CMOs, supply chain partners) are selected and sustained through a shared vision for continual improvement and excellence.
Sub-element 2h: Commit appropriate resources to implement and maintain the PQS and improve its effectiveness			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Understaffed in many critical functions. Frequent delays due to lack of available or qualified personnel. Personnel planning is insufficient to deliver properly staffed operations. Vacancies are not filled in the time needed. ☐ Production experiences frequent delays due to lack of materials for reasons within the operation's control. ☐ Systems and tools are outdated or are well behind current industry practices. ☐ Facility upkeep is not at the desired level and may even show signs of disrepair. ☐ Much of the equipment is past its useful lifespan, due to insufficient funding.

MRR Element 2: Management Commitment (continued)			
Sub-element 2h: Commit appropriate resources to implement and maintain the PQS and improve its effectiveness (continued)			
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> Partially defined Not formally controlled Not formally monitored Person dependent 	☐ Understaffed in some critical functions. Some personnel planning is conducted, and some vacant or new roles are being filled but not necessarily adhering to the plan. ☐ Production and quality transactions experience more delays than desired due to lack of available resources. ☐ Facility upkeep is mostly up to industry standard and is being maintained sufficiently. Facility, equipment, and system investments are happening, but not at the levels needed to fully maintain and sustain the operation. ☐ Reactive, unplanned maintenance is needed at a higher level than desired. There is some critical infrastructure that is past its useful lifespan, with no investment plan for improving it.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> Defined policy and processes Meets requirements for application Process monitoring and controls in place 	☐ Critical functions are adequately staffed, but there are gaps in other functions. Personnel planning is done to ensure future and vacant roles have staffing plans established. Qualified candidates are hired to fill positions within the established timeframe, most of the time. ☐ Personnel training is largely driven by meeting the compliance requirements rather than addressing talent development opportunities. ☐ Production and quality transactions occur mostly without resourcing issues. ☐ Funds for equipment, facilities, and systems are planned and tracked regularly to ensure capital improvements are completed to maintain a validated state. ☐ Systems and tools are up-to-date and adequate for the current operation; however they are not necessarily used proactively, only when an issue develops.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> Defined policy and processes Routine application Routine monitoring, advancing improvements 	☐ All functions have adequate staff. Personnel forecasting is linked to the strategy management process and translates to approved headcount plans and budgets. Key personnel (to supervisor level) are appropriately assigned, and a significant portion of indirect and fixed production personnel are assigned to products, processes, and locations. ☐ Role-based learning and development programs are in place with individual development plans used to capture and plan for future skills needs. ☐ Subject matter experts are in place for key processes but may not be fully skilled or utilized to share their knowledge on a range of related technical matters. ☐ Facilities, equipment, and systems are funded adequately for the operation, are up-to-date, and are maintained in a proactive maintenance state. ☐ Business process systems and analytical tools are advanced and in line with industry best practices and are used routinely to assess system and process effectiveness, both reactively and proactively.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> Proactive Continual improvement Predictive 	☐ Personnel planning is aligned with the Quality plan and business strategy process to attract and retain top talent and assure that the scope of roles is matched to people's current and future capabilities. Talent retention, attrition, and succession are proactively planned. ☐ With few exceptions, individuals have the necessary skills and training to perform their assigned position, with development and succession plans specific for their role. ☐ Fully capable subject matter experts are in place for all key processes and involved in curating and disseminating organizational knowledge across the business, e.g., CoPs, expert networks. ☐ Facilities, equipment, and systems are all within useful lifespans and are managed through a lifecycle management approach. ☐ Business process systems and analytical tools are not only contemporary but are part of the continual improvement process to ensure processes are effective, efficient, and remain ever-relevant to changes in the operation and regulatory trends.

MRR Element 2: Management Commitment (continued)			
Sub-element 2i: Clear standards are established, communicated, and reinforced through personal example			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Senior management's expectations and standards around Quality are not known. ☐ Low levels of trust, healthy conflict, and accountability exist.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Senior management has made some attempt to clarify expectations but sends a mixed message with decision making. ☐ Pockets of trust, healthy conflict, and accountability exist.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ Senior management expectations and standards are clear and clearly communicated. Leaders act consistently with these expectations. ☐ In general, there is an effective level of trust, healthy conflict, and accountability, although the organization is not highly effective in this area. ☐ Senior management is accountable for investing in continual process improvements and systemic improvements to make the system/process capable of meeting the required standards. ☐ Such analysis takes into account the present capability of any process or system. If a process or system is not capable of meeting the required or desired standards, then further analysis and investment in improvement of the inputs and throughputs are made to achieve the desired outputs/results.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ Leaders consistently "walk the talk" and promote a culture of trust, healthy conflict, and accountability – both top down and peer-to-peer. ☐ Leaders value and measure leading indicators, which include key behaviors, and consistently optimize and advance improvements. ☐ Use of leader standard work practices are embedded and optimized for routine tasks such as Gemba, tiered accountability processes, and metrics overview. ☐ Leaders are highly visible and accessible throughout the organization.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ A highly effective organization with high levels of trust, healthy conflict, commitment, accountability, and focus on results. ☐ There is a high level of clarity throughout the organization which is reinforced consistently, and the organization is highly empowered. ☐ All employees routinely act as owners/leaders, taking full accountability and pride in the quality of the work that they undertake. ☐ The organization is proactive, preventive, and predictive in its use of process and product knowledge to drive improvement and risk reduction.
Sub-element 2j: Quality improvement is rewarded and recognized			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Improvements to Quality systems or Quality results are not tracked. ☐ No rewards and recognitions are provided for improvements.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ There is some tracking of improvements to Quality systems or Quality metrics. ☐ Rewards and recognition of these improvements are inconsistent with no formal system in place. ☐ The system is more focused on the Quality organization.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ There is a formal system in place to track Quality system improvement projects and monitor improvement of Quality results. ☐ There is some balance of objectives between quality, cost, productivity, etc. ☐ There are some rewards and recognitions related to quality, but gaps may exist in how they are tied clearly to objectives and outcomes and/or they are not routinely visible to the organization. ☐ The system is cross-functional but with more emphasis on the Quality organization tracking, trending, and rewarding quality improvements.

MRR Element 2: Management Commitment (continued)			
Sub-element 2j: Quality improvement is rewarded and recognized (continued)			
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	<ul style="list-style-type: none"> ☐ There is a consistent balance of improvement objectives and projects between quality, cost, productivity, etc. ☐ Improvement projects have clear objectives and outcomes with accountable individuals and teams. ☐ Individuals and teams are intrinsically motivated for their efforts which are tied to the Quality objectives and the organizational core values. Reward and recognition systems promote a fully engaged organization. ☐ Success of key Quality system improvements are shared in forums led by management but may not be consistently visible to the wider organization. ☐ The recognition system for quality improvements and quality results is cross-functional.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	<ul style="list-style-type: none"> ☐ Individuals and teams are highly engaged and motivated to exceed expectations, and these behaviors are recognized by their peers and leaders routinely. ☐ The status of quality improvement projects and quality results is highly visible and championed throughout the organization. ☐ Quality improvements are clearly linked to a commensurate reduction in risk to the patient and the business. ☐ The reward/recognition system is cross-functional, consistently visible across the organization, and supports a highly engaged organization.

6.3 Assessing MRR Element 3 – Quality Planning

Senior management has a key responsibility to implement a robust Quality policy and ensure that the Quality objectives for the organization are clearly defined and effectively communicated across all functions. Where the quality planning system is more mature, all elements operate consistently across functions. Routine monitoring of leading quality indicators is used to drive proactive actions. Mature systems also routinely incorporate a standardized periodic review process that seeks to learn from issues and improve. The Quality plan goals and objectives are cascaded to employees. Continual improvement activities are included as an input to the Quality plan; these activities focus on the end user patient/consumer needs and customer requirements. Monitoring and reporting are organizationally inclusive and routine, and any action needed to stay on course is proactive.

At a minimum, the regulatory expectation for quality planning as set out in ICH Q10 [1] is as follows:

“(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.”

In organizations where quality planning is less mature, senior management may have not yet defined or only partially defined a clear Quality plan. The objectives may not be measurable or monitored. In these cases, it is common to observe that the plan is not fully deployed across the organization or the plan is only deployed to the Quality unit. Only non-routine or ad hoc monitoring and reporting processes may be in place.

The detailed evaluation criteria for the Quality Planning MRR element are provided in Table 6.3.

Table 6.3: Assessment Criteria for Quality Planning

MRR Element 3: Quality Planning			
Level 1 Undefined	Compliance risk	<ul style="list-style-type: none"> • Undefined • Uncontrolled • Not monitored • No evidence 	☐ Senior management has not yet defined a clear Quality plan nor are measurable objectives defined or monitored.
Level 2 Defined	Partially meets ICH Q10 requirements	<ul style="list-style-type: none"> • Partially defined • Not formally controlled • Not formally monitored • Person dependent 	☐ Senior management has partially defined a Quality plan and measurable objectives with some elements in place, but the plan is not fully deployed within the Quality organization or other functions; non-routine monitoring and reporting.
Level 3 Managed	Fully meets ICH Q10 requirements	<ul style="list-style-type: none"> • Defined policy and processes • Meets requirements for application • Process monitoring and controls in place 	☐ Senior management has a defined Quality plan in place. ☐ Goals and objectives are established in the plan that link to the overall quality strategy but monitoring and reporting may have inconsistencies. ☐ Continual improvement is present but may be limited. ☐ The Quality function is fully engaged in quality planning with limited participation by other functions.
Level 4 Improved	Demonstrates improved/ optimized execution	<ul style="list-style-type: none"> • Defined policy and processes • Routine application • Routine monitoring, advancing improvements 	☐ A clear Quality plan is established across functions with increased focus on continual improvement; monitoring and reporting of the plan's goals and objectives is routine but perhaps not fully organizationally inclusive – primarily led and owned by the Quality function. ☐ A robust periodic review process is in place to learn from issues and improve. ☐ Routine monitoring is in place, and leading indicators are used to drive proactive actions.
Level 5 Optimized	World class/industry leader	<ul style="list-style-type: none"> • Proactive • Continual improvement • Predictive 	☐ The quality planning system is mature with elements operating consistently across functions; goals and objectives are typically meeting or exceeding intent. ☐ The Quality plan goals and objectives are cascaded to all employees and activities are linked. ☐ Continual improvement focusing on the patient/consumer is included as an input. ☐ Monitoring and reporting is organizationally inclusive and routine. ☐ Proactive measures to stay on course or adjust course for the Quality plan are routinely undertaken.

6.4 Assessing MRR Element 4 – Internal Communication

The strength of the quality management process relies heavily on transparent communication of all relevant quality activities. ICH Q10 [1] states:

“(a) Management should ensure appropriate communication processes are established and implemented within the organization.

“(b) Communication 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.”

In more mature organizations where communication expectations are clearly established and formally monitored for both implementation and effectiveness, a *speak up* culture (i.e., a culture where employees are encouraged to positively communicate concerns) is generally observed to be in place. Internal communications openly share external perspectives from regulators and patients/consumers as well as internal perspectives from employees through *voice of the stakeholder* processes. Organizational knowledge such as best practices and lessons learned are formally captured and shared, and forums exist for cross-functional heads to share challenges and successes.