



The perfect quality assurance plan for pharmaceutical companies

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Processes, systems, and company culture

Quality assurance is a broad concept in the pharmaceutical industry. It involves the review of all aspects that can have an impact on patient outcomes. For a pharmaceutical company, quality is closely connected to current Good Manufacturing Practice (cGMP), which helps your business produce pharmaceuticals which meet customer requirements for quality, strength, and reliability. Without a comprehensive QA plan, your pharmaceutical organization cannot demonstrate compliance or ensure products conform to quality or safety standards.

The risks of failing to implement a comprehensive quality system are well-documented. Organizations can incur internal costs related to product failures and remediation. External costs can include regulatory action, loss of market share, and reputational damage. [An academic study](#) found that QA failures can result in business costs over \$100 million. For the small percentage of big pharma firms that face litigation, the costs can exceed \$1 billion.



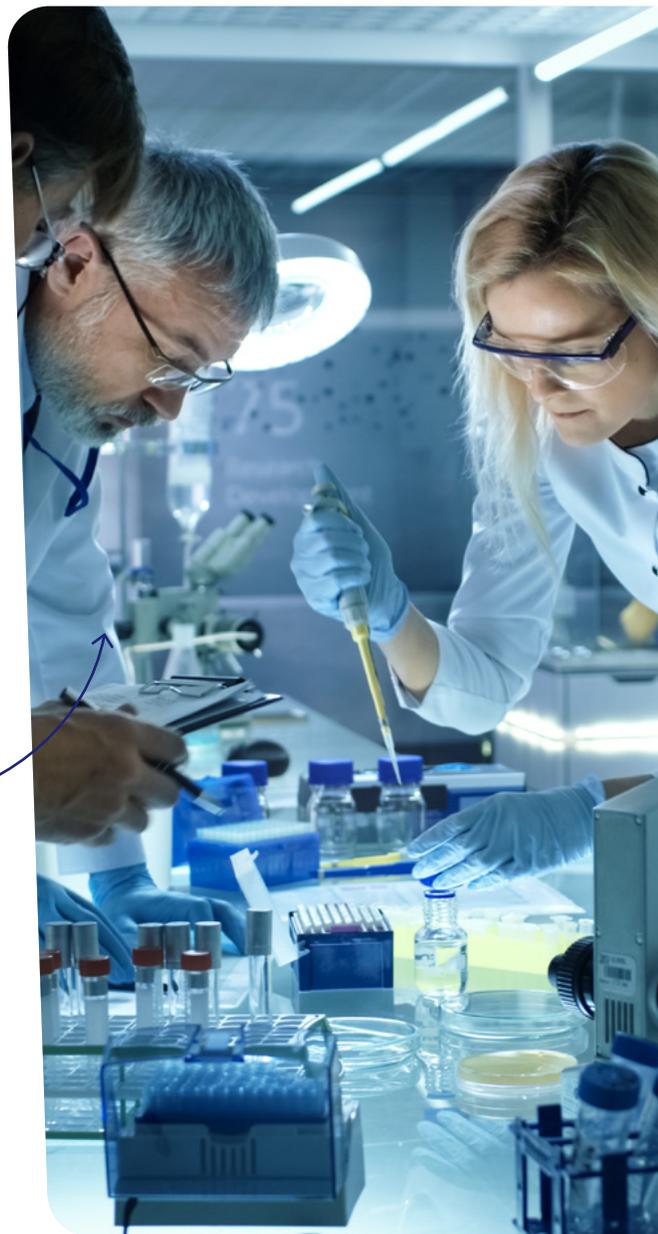
A lack of quality control can impact the entire organization, but in whose court does the responsibility lie? Creating an effective quality management plan is generally the responsibility of the QA department at pharmaceutical organizations. However, a highly effective plan will have a significant impact on every branch of the organization and create momentum toward a quality-driven culture. The plan should address every element of the process which can impact patient outcomes and satisfaction, including development processes, raw materials, manufacturing process, packaging, transportation, and storage. The plan also shapes software and systems, training, and accountability of all members of the workforce.

While creating a comprehensive quality management plan is no small undertaking, studies consistently confirm that QMS is a valuable activity for pharmaceutical companies in today's complex competitive climate. One study of ISO 9001-compliant organizations found "when an organization applies the quality concept to its processes and its entire management system... it is able to see an effect on its bottom line." Quality efforts help you make more consistent products while increasing efficiency and reducing expenses. It's just good for business.

When an organization applies the quality concept to its processes and its entire management system... it is able to see an effect on its bottom line.

Building the perfect pharmaceutical QA plan

In this guide, you'll learn how to create a perfect quality assurance plan for your pharmaceutical organization which unites processes, systems, and culture. A "perfect plan" can reduce regulatory risk and enable your company to become a quality-driven organization.



Processes

Understand the regulations for pharmaceutical companies

Regulatory requirements should be the first consideration for any pharmaceutical organization creating a quality management plan. This includes start-ups and scale-ups who are in the early stages of drug development. While the organization may not yet be at risk of corrective action from regulatory bodies, a comprehensive understanding of regulations still matters to create systems which scale and comply in the future.

US-based pharmaceutical organizations should work to assess and understand the following regulatory requirements from the Food and Drug Administration (FDA), including clinical requirements:

- Code of Federal Regulations (CFR) Title 21, Part 210: [Current Good Manufacturing Practice](#)
- CFR Title 21, Part 211: [Current Good Manufacturing Practice for Finished Pharmaceuticals](#)
- CFR Title 21, Part 11: [Electronic Signatures for Electronic Records](#)
- 21 CFR, Part 50: [Protection of Human Subjects \(Informed Consent\)](#)
- 21 CFR, Part 54: [Financial Disclosure by Clinical Investigators](#)
- 21 CFR, Part 56: [Institutional Review Boards](#)
- 21 CFR, Part 58: [Good Clinical Practice and Clinical Trials](#)
- 21 CFR, Part 312: [Investigational New Drug Application](#)
- 21 CFR, Part 314: [Applications to Market a New Drug](#)

If your marketing ambitions post-approval include Europe, you should strongly consider aligning your quality system to ICH Q10 earlier in your development.

The basics of your quality plan

- Document control
- Training
- Deviation
- Laboratory OOS
- CAPA
- Internal audits
- Management review

A comprehensive quality plan will provide a full foundation for compliant manufacturing systems. Each of the subsystems integrate and work concurrently to achieve the organization's goals of consistently producing quality pharmaceuticals.

Document control

All FDA-regulated and ISO-certified companies are mandated to have a system for document change and control. The FDA's current Good Manufacturing Practice (cGMP) guidelines and ISO quality standards presume that processes follow pre-approved methods, and changes are restricted to authorized personnel and tracked for review. A comprehensive document control system should be implemented in the earliest phases of the pharmaceutical organization to create a stable baseline of compliant

documentation in case of FDA inspection.

A document management system creates efficiency and eases regulatory compliance by eliminating the excessive paper and difficult tasks of physically managing documents. The plan will address the entire document lifecycle, including stages of draft, release, and archival and support the use of audit trails to capture changes and change metadata. The plan should additionally address the use of secure storage systems, access authorization, disaster recovery, and the linking of documents to simplify workflows.

Training

FDA notice of violation letters frequently note a lack of training or a need for retraining in CAPA improvements. In one recent year, [30% of warning letters](#) issued by the FDA for data deficiencies referenced training. Effective training requires a quality plan to create a culture of quality assurance throughout the pharmaceutical organization.

The training plan includes guidance for each of the primary roles, including curriculum for new hires, current staff members, contractors, and the individuals responsible for overseeing training. Creating a training plan based on roles can enable the development of a curriculum

directly from the standard operating procedures (SOPs).

In addition to role-based training, the quality plan should address ongoing employee monitoring, including organizational key performance indicators (KPIs) for employee assessments. Creating a culture of continuous improvement can be vital to implementing an appropriate focus on training.

Deviation

For compliance to GMP mandates, pharmaceutical organizations are required to document any deviation from SOP or other specification or requirement, such as test specs for raw materials or finished goods, etc.

FDA § 211.192 requires that any deviations are thoroughly investigated and followed-up on, including documentation of the investigation and findings. The deviation SOP will address methods to identify and record deviations, and procedures for investigating incidents.

The quality management plan for deviations addresses:

- Real-Time deviation reporting
- QA notification within 24 hours
- Root cause investigation within 30 days

- Procedures for proposing and implementing corrective actions
- Standards for concluding an investigation
- Policies for rejecting deviated batches
- Initiation of preventive actions

Laboratory OOS

Investigating OOS laboratory results is mandated for GMP pharmaceutical organizations. The quality plan should contain a comprehensive plan for investigating the root causes of results which are not aligned with expectations. When an OOS value is discovered, the policy should dictate steps for determining the root cause and corrective action.

OOS investigations are among the top causes of FDA warning letters. The quality management plan must address the design of an investigation plan, timelines, responsibilities, and acceptance criteria. Elements to incorporate in a laboratory OOS quality management plan include:

- Identifying OOS test results
- Laboratory investigations
- Root cause identification, CAPA, and follow-up
- Determining course of action to process analytical methods for monitoring product trends

- Investigation plan design
- Investigation acceptance criteria
- Investigation report policies and components
- Timelines, roles and responsibilities
- Corrective and preventive action (CAPA) policies
- Determining KPIs for process monitoring

CAPA

Corrective and Preventive Action (CAPA) is a complete system to support self-correcting quality systems within the organization. A comprehensive quality plan for CAPA can enable pharmaceutical organizations to assure quality issues are resolved, reduce customer complaints, maintain regulatory compliance, and adopt a structured approach to solving problems.

The plan for CAPA should address each component of the system, including the identification, evaluation, investigation, and determination of resolution plans.

- Identification is the process of collecting facts on the event, date, and time.
- Evaluation works to address the impact on customer safety, regulatory compliance, and process.

- Investigation attempts to identify a root cause.
- Determination of resolution prescribes correction, corrective action, or preventive action.

The fifth and final stage of a CAPA plan prescribes methods for determining the efficacy of corrective actions and the documentation of these safeguards. The plan should address the importance of applying timely action and the review of data or use of audits to ensure the quality system is functioning.

Internal audits

Internal audits are a valuable tool for compliance and identifying issues before they cause quality problems or customer complaints. The quality management plan defines audits as an ongoing tool for process improvement and employee training. ISO 9001 dictates "internal audits at planned intervals," while [FDA guidance](#) for pharmaceutical organizations places audits within the required record review process to evaluate "the applicability of quality standards, need for changes in specifications, manufacturing processes, or control procedures."

The audit plan addresses audits for quality systems, packaging, labeling, suppliers,

material controls, facilities, training, and complaints:

- An audit schedule which covers all critical areas each year
- Audit scope
- Processes for addressing issues

Management review

Integrating a system for management review into the quality plan is a tool to ensure quality management systems are owned by pharmaceutical leadership. Management review is a requirement of ISO 9001 and dictates regular meetings between the leadership team and process owners to discuss improvements to quality systems, processes, products, and planning.

[FDA guidance](#) on management review addresses the following management activities during the regular review:

- The appropriateness of the quality plan for the organization
- Audit and assessment results
- Customer feedback and complaints
- Data analysis, KPIs, and metrics
- The status of corrective or preventive actions

- Changes to the environment or practices which may impact quality systems
- Customer satisfaction and product characteristics

The quality plan should address the required agenda items for each management review session, attendance requirements by role, and how frequently the meetings should be held. We will cover more on management reviews in part 3.

Comprehensive GMP

The documents which comprise the quality management plan should be controlled for FDA GMP around the following factors:

- The facility, including calibration, validation, and maintenance records
- Equipment, including manufacturing calibration, validation, and maintenance records
- Laboratory, including equipment calibration, validation, and maintenance records
- Drug substance, such as supplier quality assurance processes for raw materials
- Drug product, including the final CMO if production is outsourced and production batch records

If your pharmaceutical organization is outsourcing manufacturing, many of these documents will be primarily housed at the CMO, since your organization doesn't have a facility or equipment to maintain. Outsourcing organizations should address processes for document review and collection from partnered CMOs.

The pharmaceutical quality manual

The quality manual is the basis for the pharmaceutical organization's quality system. It unites processes with the product and prescribes a clear plan for meeting all applicable regulatory requirements and standards. A pharmaceutical quality plan should be fully described in the manual, carried out in SOPs, and proved through records generated.

Scaling a useful quality manual for drug development processes requires pharmaceutical organizations to start with a focus on effective systems for document control and training, and scale to address other requirements such as CAPA and audits. With a system that enables ease of configuration, organizations have the freedom to build out the necessary pieces and add new elements as the pharmaceutical organization scales up.

The characteristics of the perfect pharma quality assurance plan

Implementing a highly effective plan for quality assurance is among the most critical goals of pharmaceutical organizations at any stage. An effective plan fully addresses quality assurance and controls toward organizational goals of producing high-quality and safe pharmaceuticals. An effective program should place quality as the organization's primary purpose and dictate clear steps towards total quality management (TQM).

The most effective pharmaceutical quality assurance plans unite action with strategy, support alignment with regulations and standards, and inform culture.

1. Alignment with strategy

The QA plan should be aligned with the organizational strategic plan, including goals for development, production, and customer satisfaction.

2. Alignment with framework

The ideal QA plan streamlines the process of certification with apparent ties to the organization's selected quality framework.

3. Continually improving

The annual QA plan represents a natural progression from the previous years' quality plan, if available, to demonstrate a commitment to continual improvement.

4. Accessible

A QA plan is accessible and easily understood by all stakeholders. Use terms that are clear to the entire workforce and members of the public.

7. Frequently evaluated

The QA plan should be subject to formal review and improvement on a regular basis, at least once per year.

5. Measurable

Whenever possible, the QA plan will track measurable goals for performance and quality, such as KPIs for training, customer satisfaction, and other aspects of the quality management system.

6. Targeted

When indicators of quality are measured, the QA plan should include targets for organizational performance and improvement.

8. Feasible

The plan should prescribe realistic processes and policies for managing quality, based on the organization's actual resources for talent and capabilities.

9. Helpful

The success of a QA plan can be measured by impact, including the effects on both people and processes. The most effective plans can create a permanent change towards a quality-focused culture.

Systems

The concept of the modern QMS was developed over 30 years ago when the adoption of technology and software were limited to the legacy systems of the world's largest pharmaceutical organizations.

In the decades since the advent of the cloud, technology has shifted the role of software in QMS to a place where the terms are nearly synonymous.

Systems play an integral role in the implementation of a QA plan. The American Society for Quality (ASQ) defines a QMS as a "formalized system that documents processes, procedures, and responsibilities for achieving policies and objectives." The QMS should help coordinate and streamline your pharmaceutical company's efforts to meet regulatory requirements and achieve customer satisfaction while contributing to continuous improvement efforts.

Selecting the right technology to power your QMS is a critical decision for pharmaceutical companies at every stage. Start-ups in the earliest drug development phases should consider lightweight systems which enable compliant scaling to avoid having to replace systems in the future and increase the company's value during a sale. Small and mid-sized organizations should evaluate their needs for customization and flexibility when examining options.

The primary role of a QMS is to support the organization's goal of creating a quality-driven culture. The software should align with the quality management plan and regulatory requirements to simplify quality-focused workflows among global stakeholders.

Selecting a QMS to implement a quality assurance plan

Cloud-based, scalable quality management systems are generally the best choice for the majority of small to mid-sized pharmaceutical organizations. Cloud-based QMS offers efficiency, ease-of-use, and simple global access for suppliers or other outside parties. Across industries, [cloud app adoption](#) continues to grow, with 81 percent of organizations using at least one cloud-based service.

The pharmaceutical industry has been comparatively slow to adopt cloud apps and services, though recent studies confirm adoption is quickly reaching the levels of less highly regulated industries. Previously, many pharmaceutical organizations faced barriers related to regulatory and quality system standards for access controls. As cloud technology has continued to mature, pharmaceutical organizations are discovering that the cloud can simplify workflow management and improve transparency. Today, more than [8 out of 10 pharmaceutical companies](#) are using at least one cloud app.

The best system for your organization will support and simplify compliance with all applicable regulatory standards. While the “best” system can vary depending on your organization’s size, there are a few nearly universal factors which can shape the impact of QMS software on culture and performance. These include simplicity, ease-of-use, and scalability.

1. Simplicity

A lean QMS offers simple customization and configuration without requiring the use of custom code. Not only does simplicity lower the costs of information technology (IT) development and dependence on third-party software experts, it reduces the requirement to meet process revalidation requirements from certifying bodies.

2. Ease-of-use

The ease of use of QMS software is defined by the extent to which the software simplifies the process of meeting regulatory requirements, streamlining workflows, and end user satisfaction. The system provides role-based access for global stakeholders based on position requirements to support global adoption. It will also simplify the QA team and management processes by providing data dashboards for tracking issues, trends, and training in real time.

Ease of compliance is generally accompanied by robust document management capabilities which scale from early-stage requirements to FDA inspections, including compliant features for digital signatures.

3. Scalability

The scalability of QMS software is a particularly critical factor for start-ups and scale-ups to consider. As your organization exits the development phase and begins to bring products to market, the role of QMS software can evolve from document control to compliance, CAPA, and other attributes.

When evaluating systems, consider how the role of the software will change as your organization's use cases expand. The features of a QMS for an early-stage pharmaceutical start-up support compliant documentation for FDA inspection and other build-outs.

Company culture

When discussing company culture, we always want to emphasize that a shift in mindset needs to occur. Unfortunately, some pharmaceutical companies overlook the real value that shifting from a compliance-driven culture to a quality-driven culture brings. It's good for business.

Sometimes pharma organizations want to become quality-driven, but there are technological roadblocks. The quality team may lack access to the data they need to make decisions and improve performance. Key team members and the broader employee base may not be engaged because a patchwork selection of tools makes it difficult to get to the information they need and contribute.

With this approach, executive-level buy-in is difficult to attain. If quality is perceived merely as a compliance necessity, the perceived ROI will not be high enough for the C-suite to invest in the changes

required to get results. But when quality is viewed as a profit-driving force for competitive advantage, the actual ROI is higher, and the company as a whole can realize significant changes and growth. Executives begin to understand that investing in the right pharmaceutical eQMS is important (that's where we come in) and devote resources to employee training and engagement for quality. In actuality, more and more pharma companies are making this shift and those who don't will fall behind.

Now let's look at the nuts and bolts of management review.

Management review and continual improvement

Management review of the QA is an essential activity on at least a quarterly basis. The results of management review meetings and CAPA program results should enhance continuous improvement

efforts. Leadership involvement is critically important to set KPIs for quality and make strategic decisions based on the current state of the QA plan and QMS.

The QA plan and QMS system should define the role of management review, goals for review meetings, required attendees, and provide a format for discussion. The necessary elements of the management review should include:

- A clear agenda and record of attendance
- Safety data and metrics review
- Customer and internal feedback review
- Objective measurements of supplier performance
- Discussion of strategic and quality initiatives
- Training and process performance and progress
- Talent and human resources discussion
- Addressing new regulatory requirements
- Analysis of changes which could impact the QMS
- Recommendations for continuous improvement
- Scoring and assessment of management quality objectives
- Establishment of new targets based on meeting discussion

To meet both regulatory and quality system requirements, documentation of the meeting should be stored in the quality management system to support future audit activities.

Creating a plan for a quality-driven culture

A perfect quality assurance plan for pharmaceutical companies is more than just a document produced by the QA team to shape SOPs. It's a comprehensive guideline for making the shift to a quality-driven culture, complying with regulatory requirements, and establishing systems of continual improvement.

Quality assurance and quality management systems can collectively define the organization's approach to total quality management, and help your company achieve its strategic objectives. An effective plan aligned with a suitable eQMS platform can prevent waste, support timely drug registration, and provide dramatic operational benefits to the entire organization.

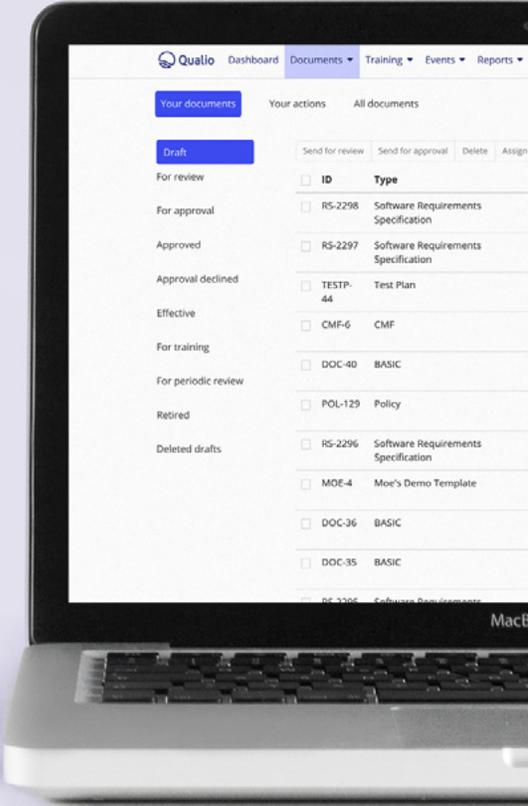
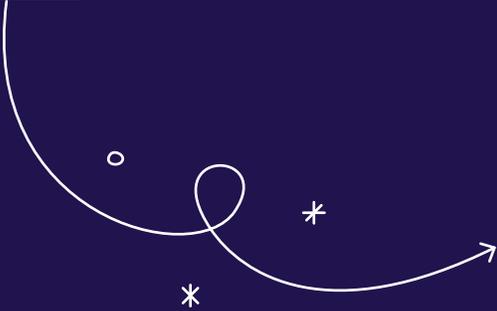


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