CAPAs, Deviations, and Investigations

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AZZUR GROUP

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Executive Summary

The constancy of change in the biotech, medical device, and pharmaceutical industries highlights a singular, unchanging truth:

The efficacy and robustness of a Quality Management System (QMS) are central to a company's success. As we anticipate the harmonization of FDA and ISO standards, the continuous improvement aspect of a QMS becomes increasingly crucial and warrants significant attention.

The Driving Force of Improvement: CAPA System

At the heart of any QMS improvement effort lies the Corrective and Preventive Action (CAPA) System.

CAPA draws its input from a variety of sources, including but not limited to internal and external audits, customer complaints, procedural and process deviations, non-conformances related to suppliers or vendors, identified trends, and management reviews. A well-constructed CAPA is among the most critical documents a company can produce. It not only details the rationale and reasoning behind improvement decisions but also demonstrates a company's commitment to enhancement. The CAPA process is rooted in factual and data-driven analysis, focusing on risk assessment, impact evaluation, and mitigation.

There are two primary approaches within the CAPA process: Reactive (Corrective Action) and Proactive/Interpretive (Preventive Action). Solidifying these processes is vital for maintaining the integrity and effectiveness of a QMS. During audits, the CAPA System is often scrutinized as a measure of the overall health of the Quality System. Its effectiveness in promoting QMS health hinges significantly on two key QMS components: investigations and comprehensive internal audits.

- Complaints/Feedback/Recalls
- Regulatory Audits
- Third-Party Audits
- Supplier (SCARs)

External Feedback

CAPA System

Internal Feedback

- Internal Audits
- Managment Review
- Nonconformances/Deviation Invesigations
- Adverse Trends

The Role of Investigations in Problem Solving

Investigations aim to uncover the "what," "when," "where," and "how" to ultimately ascertain the "why" or root cause of a problem.

A skilled investigator, often leading a team, uses gathered facts and tools (such as failure modes or fault tree analysis) to determine the root cause. Understanding the root cause is pivotal for deciding the most effective corrective or preventive actions. The development of a CAPA is based on this root cause analysis, with involvement from relevant experts, departments, and management, each providing reviews and approval. Post-implementation, an effectiveness check ensures that the actions taken effectively prevent recurrence or occurrence of the identified issue. If ineffectiveness is noted, the CAPA process is revisited until a resolution is achieved.

Not every identified issue necessitates a CAPA, however. The responsibility of making this determination falls to the investigator using policies and the investigation process. Investigators, equipped with the right mindset, must manage deviations, non-conformances, and complaint investigations efficiently to mitigate risks and uphold product and process quality. The investigation process should adopt a risk-based approach, gauging the depth of investigation needed as well as the complexity of the problem under investigation. This involves risk identification, analysis, and prioritization, followed by efforts to minimize, monitor, and control the likelihood or impact of adverse outcomes. The scope of the problem aids in the assessment of the risk, considering factors like the number of affected lots, locations involved, product distribution, occurrence frequency, and identification in Failure Mode and Effects Analysis (FMEA) or Hazard Analysis. Statistical techniques such as Pareto charts, run charts, control charts, etc., may also assist in determining the necessity for a CAPA.

The Importance of Comprehensive Internal Audits

Another crucial component of the CAPA loop and an effective QMS is a comprehensive internal audit program.

This program challenges the adequacy and effectiveness of a company to run under the oversight of the QMS, including evaluating compliance with internal procedures, policies, and applicable regulations (FDA, ISO, etc.). Comprehensive internal audits are designed to periodically evaluate the entire scope of the QMS, at a schedule and frequency that may be dictated by using a risk-based approach. This approach should consider potential business or product impact and past audit outcomes. Internal audits are an integral part of the improvement process, aimed at identifying gaps or deficiencies within the QMS, which may be further documented and investigated using the CAPA process for implementing effective changes or additional monitoring to assure that important improvements are made in critical areas.

A successful audit, conducted by a competent auditor, is crucial for problem identification and identification of areas of improvement. An effective audit should be unbiased, systematic, standard or regulation-based, and objective. The auditor's goal is to collect evidence to evaluate whether the existing systems are functional and effective, compliant with internal and external requirements, and pinpoint opportunities for improvement or optimization. The audit process facilitates solutions through comprehensive communication, discussions in the closing meeting, a well-structured audit report, and feedback on audit responses. The closure of an audit often hinges on evidence of the completion of actions defined in the audit responses, effectiveness checks on any changes, and monitors for unintended consequences, all of which feed into the CAPA process for continual improvement.

The Feedback Loop in QMS: A Key to Success

An effective QMS relies on precise and timely feedback.

It is not always feasible to preemptively prevent problems or to achieve perfection on the first attempt. Therefore, establishing a feedback loop, supporting investigation processes, and maintaining a system that fosters improvement throughout the business and product lifecycle are critical for the health and success of the QMS. This loop allows a company to regularly monitor and review its processes, evolve with changing regulatory requirements, and consistently focus on improvement and quality. While regulatory agencies provide the foundation for quality systems through requirements and guidelines, it is incumbent upon companies to operationalize those requirements within their businesses through optimization of the QMS, always quality, effectiveness, and safety for the end user in every decision made.

A QMS, fortified with an effective CAPA system, thorough investigations, and comprehensive internal audits, fosters a culture of continuous improvement and forms the backbone of any successful organization. As the healthcare industry continues to advance and integrate new technologies and methodologies, the role of a dynamic and responsive QMS becomes even more vital, underscoring its importance in maintaining industry leadership and ensuring the delivery of safe and effective products to end users worldwide.

About Azzur Group

From Discovery to Delivery™, Azzur Group provides the life science community full life-cycle solutions for all of their GxP needs.

From Azzur Cleanrooms on Demand™ facilities, to our labs, training centers, and consulting offices across the nation, Azzur Group helps organizations start, scale, and sustain their growing enterprises. With nearly four decades of service to the life science community, we have become a trusted partner to the world's leading pharmaceutical, biotechnology, medical device, and healthcare companies, as well as their supply chain.

For more resources on this topic, or to learn about solutions Azzur Group provides to organizations in the life science community, visit our website.

About the Authors

About the Author: Eliza Deriso

Eliza Deriso is a seasoned professional with a strong background in quality management and auditing. With a career spanning over a decade in both the automotive and life science industries, Eliza has amassed extensive experience in driving quality initiatives. Following a transition from the automotive sector to the life science industry, Eliza joined Azzur Group in 2021, and now leads an audit program that encompasses GMP, GLP, GCP, Medical Device, and Mock FDA audits, among others.

About the Author: Steve Masi

Steve Masi has nearly 30 years of experience in design, development, manufacturing, quality of implantable and non-implantable medical devices in a regulated cGMP environment. He also has experience working in the pharmaceutical industry and has a working knowledge with the associated ICH and FDA regulations.

Since 2005, Steve's area of expertise has been primarily rooted in the medical device field in R&D, manufacturing, and quality. He has worked with products such as brain and spinal implants used in drug delivery, diffusive membranes, colonoscopy products, voice prostheses and accessories, breast implants, wound adhesion products, proton therapy systems, and electroporation systems for drug delivery. He has also worked on quality teams in support of critical utilities supporting medical device and pharmaceutical manufacturing operations. During his time at Azzur Group, he worked on the creation, implementation, maintenance/support, and gap assessments of phase-appropriate quality systems, as well as quality support for pharma and medical device organizations.

About the Author: Jeffrey Silverman

Jeffrey Silverman is a former Vice President of Product Engineering and Manufacturing for OncoSec. As an engineering management veteran, Jeff has extensive global industry experience in the development, manufacturing, and scale up of medical devices including electroporation and gene delivery equipment for the delivery of DNA drugs in support of cancer and vaccine research.

For more than five years, Mr. Silverman served as Vice President at Ichor Medical Systems, Inc., an industry leader focused on the development, manufacture, and sale of electroporation devices for the intracellular delivery of nucleic acid-based drugs encoding therapeutic proteins. While at Ichor, he was responsible for establishing and leading the engineering, operations, and quality teams for the company's electroporation equipment for the delivery of DNA drugs in support of cancer and vaccine research. Mr. Silverman was also responsible for engineering design execution and planning, supply chain, supplier audits, internal, and external manufacturing and contract coordination.

Prior to joining Ichor Medical Systems, Mr. Silverman was the Managing Director at Varioscale, Inc. Adding to his past experience, he held a variety of engineering and business manager roles, including his time at Abbott Laboratories and Guidant Corporation where he managed business alliance, program management, business excellence, engineering/manufacturing process development, and systemic improvements.