Medical Device Communiqué

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THE ART OF EFFECTIVE CAPA AND FOLLOW-THROUGH

The experts at Compliance Insight (www.compliance-insight.com) maintain our CAPA courses, including our course on FDA's QSIT process related to CAPAs, QSIT 4 -- The Corrective and Preventive Actions Subsystem. In this article, they share CAPA followup best practices.

As professionals in a well-regulated industry, we have been hammered over the head with the old adages "Don't make promises you can't keep, It's not the quantity but the quality that matters, Do it right, do it once..." What if deviations occur? How can we ensure that corrective actions work? What is the best way to prevent incidents? The FDA is depending on Quality personnel and industry leaders to provide innovative insight into improvement strategies and data that supports their effectiveness.

Defining Procedures and Focus on Continuous Improvement

If your procedure on maintenance and review of SOPs does not establish a realistic yet aggressive process for updating and evaluating your procedures, you may want to rethink the strategy. The accuracy and enforcement of procedures is a must. Your first line of defense when called into an inspection are those documents that show you have proper control over your processes, a.k.a. your SOPs. Additionally, identifying continuous improvements prior to deviations lowers the risk of non-compliance and provides an action plan. Make sure your procedures are understandable and properly trained upon with a standard review cycle (generally no longer than biennially).

Incorporation of Risk Management Methodology

You might think that risk assessment is directly involved in CAPA and changes to systems and procedures, but it also helps with new procedures and systems as well. Think of Design Control as a good example. Risk assessment strategies can allow for thorough evaluation prior to implementation (what effect will this have on current systems, will changes be necessary down the line, etc.). So, minimizing sterilization time may speed up production, but will it have an effect on the finished device? Will it affect product quality and storage? These strategies help in the Proactive as well as the Reactive approach and are vital to proper change management.

Follow-through and Evaluation of CAPA Effectiveness

We've evaluated all deviations and areas for potential change, and we've implemented all of our corrective and preventive measures, so now what? Do your procedures define parameters and a time period for ensuring the changes were effective? Have the SOP revisions helped? Was the CAPA written with the evaluation of effectiveness in mind? Effectiveness checks should be procedurally driven, managed by Quality Assurance and include the personnel involved in the original corrective actions, along with other subject matter experts. Incorporating review of systems or products into an annual review is one way to ensure updates have been properly executed. Internal audits can also be used in this way to confirm the effectiveness of changes or newly implemented systems. They also help keep our heads in the game, similar to periodic training, like a pop quiz[1].

Consistent and Timely Quality Training

Training on procedures must be current and can definitely assist in preventing deviations, but what about focusing on the basics? cGXP training is critical when it comes to keeping a focus on quality. And here we can't forget that quantity matters too. Annual training is helpful, but taking time throughout the year to discuss topics pertinent to each area and associated personnel will keep heads in the game and act as good reminders.

Ensure Quality and Timely Documentation

Recently, we have assisted clients with FDA responses to observations and warning letters. Many of the observations and associated corrective actions could have been avoided with a well-

THE ART OF EFFECTIVE CAPA AND FOLLOW-THROUGH *(Continued)*

developed and specific procedure on good documentation. There is no better way to confirm the quality of a product than to review a firm's documentation, hence the prolific process of FDA inspections. Quality documentation is a must, and it goes without saying that processes must be documented at the time they occur, rather than later. Too many observations are defined for lack of or improper documentation on batch records, laboratory notebooks, log books, etc. Getting caught with poor documentation practices in front of an FDA inspector leaves many Quality personnel scrambling for excuses.

Looking Forward – The Proactive Approach

In the recent past, FDA inspectors have cast a critical eye on CAPA resolution with emphasis on recurrent deviations post CAPA. Having control over your deviation and corrective action systems means taking a more proactive approach to continuous improvement, which should be based upon quality data such as:

- Data trending and holistic data reviews
- Continuous Improvement Projects
- Industry and Regulatory Surveillance
- Cost of Quality Model
- Implementation of CAPA earlier in the development

A well-developed Quality System can provide this data integrally collected and analyzed by keen eyes. Many electronic data systems have been developed for companies of all sizes that will provide statistical data on corrective actions, including cause and recurrence[2].

While Quality personnel are the leaders in maintaining high levels of product quality and driving continuous improvement, it is important to remember that everyone from the highest level of site management to the newest personnel in shipping are key players in the quality infrastructure.

References:

1. Compliance Insight, Inc. Presentations: CAPA TRAINING PRESENTATION ©2013 via Slideshare.net.
2. CH Q10 Conference Presentation: CAPA within the Pharmaceutical Quality System, October 2011 presented by Martin VanTrieste, R.Ph, SVP Amgen

FDA WARNING LETTER AND 483 OBSERVATION TRENDS

The following article was written by the experts at Compliance-Insight (www.compliance-insight.com), which maintains a number of our medical device GMP and QSR courses, including our Complaint Management course (DEV46).

MFDA Warning Letter and 483 Observation Trends

One way the Food and Drug Administration provides feedback and guidance, as well as enforcement of current regulations, to manufacturers and associated industry groups is through the inspection process. The evidence of an inspection is documented and communicated in heightening levels of severity from the close out meeting, FDA 483 forms to an official Warning Letter. We will discuss current trends in observations and inspection findings in the following paragraphs.

Inspection Statistics

The agency reportedly issued nearly 5000 FDA-483 forms with observations in 2015, over 20% of these observations were given to Medical Device manufacturers, distributors and associated facilities.[1, 2] To ensure a robust and current Quality System, it is critical that the Quality department stay up to date on these observation trends, as well as understand when these will turn from findings to enforcement actions.

Failure to Establish Procedures

Inadequate or lack of established procedures was the driving force behind the top 5 observations cited in 483s for 2015. While failure to establish corrective and preventive action procedures was top of this list, lack of reporting and follow-through in complaint investigation encompassed a majority of these observations. For example:

Failure to develop, maintain and implement written medical device reporting (MDR) procedures, as required by 21 CFR 803.17. Specifically, the procedure does not establish internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements.

You must establish a realistic yet aggressive process for updating and evaluating your procedures. Your first line of defense when called into an inspection are those documents that show you have proper control over your processes, a.k.a. your SOPs. For more information on SOPs, see “GMP Principles of SOPs” (PHA64) as well as “Writing and Reviewing SOPs” (PHA48).

For MDR specifically, the FDA has defined and clarified the

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FDA WARNING LETTER AND 483 OBSERVATION TRENDS *(Continued)*

requirements to thoroughly investigate adverse events, complete the required forms and submit reports to the agency ad nauseam. These are basic expectations of the Quality System, both the reporting and the development of your procedures.

Failure to Validate per Established Procedures

Failure to validate, with a high degree of assurance and approve according to established procedures, a manufacturing process that cannot be fully verified by subsequent inspection and testing, to ensure the process will continue to meet specifications as required by 21 CFR 820.75(a).

Once you implement a procedure that meets regulatory requirements, say for validation of manufacturing processes or qualification of equipment prior to use in a GMP environment, inspectors will insist that the procedures be followed. The intent of Validation is to confirm the ability of those processes and equipment to consistently and effectively produce quality devices. Revalidation may be necessary to show that any changes to the process have no negative impact on the product quality. Inspectors will insist on documentation of validated processes and qualified equipment, so it is best to have both the procedures and validation documentation readily available for inspection. For further training on validation concepts, please see "Documenting Validation Activities" (PHA55) and "Writing Validation Protocols" (PHA51).

Devices Requiring PMA

A review of the FDA Premarket Approval (PMA) database revealed that (the company) does not have any approved PMA to market a device in the United States after your firm transferred (sold) (the device) in March 2009. For a device requiring premarket approval, the notification required by section 510(k) of the Act, 21 U.S.C. 360(k), is deemed satisfied when a PMA is pending before the agency. 21 C.F.R. 807.81(b).

For manufacturers caught unaware, the filing process for Premarket Approval may be daunting and responsibilities may not be clear. That said, FDA inspectors have made it clear that if the application is deficient or unavailable at inspection, the device may be considered adulterated initiating action by the agency.

Documentation and Training

Additionally in 2015, hundreds of 483 observations were recorded by inspectors for lack of documentation and training. Current documentation for Design History Files and Device Master Records, including design change control documents, risk assessment and corrective action reports, along with any associated training forms, is critical for each device produced.

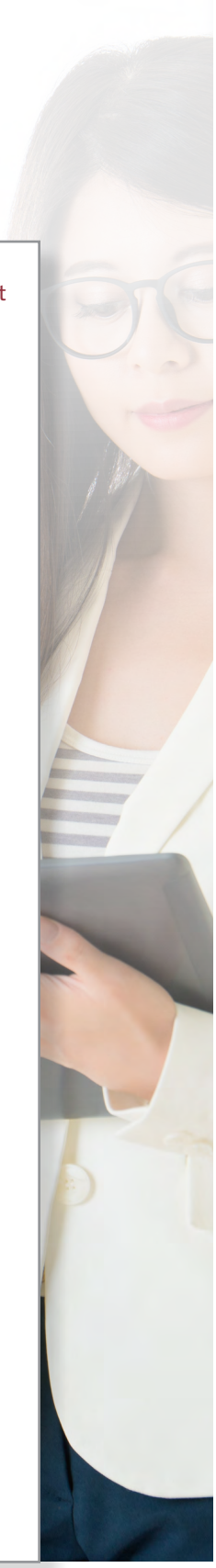
The ability of a firm to continue to market, import and/or produce quality medical devices within the United States is directly proportional to their ability to properly document and provide evidence of product quality during an inspection. Documentation failures and gaps cause uncertainty and violate the regulations defined by the FDA and are therefore actionable offenses. For further information on proper documentation and required training, please see "Principles of Good Documentation" (PHDV65) and "FDA Training and Qualification Requirements" (PHA67).

A clearly defined and effective action plan is critical for any response to a Warning Letter or 483 Observations. For more information regarding responding to inspection findings, please see "Effectively Responding to FDA 483s and Warning Letters" (PHDV70).

References:

1. www.fda.gov
2. FY 2015 Inspectional Observation Summaries, published January 22, 2016.

MANAGEMENT REVIEWS: SAMPLE CHECKLIST



The following article is an excerpt from our new course, Management Responsibility for Quality: What FDA Expects (PHDV101), which was written by the experts at EduQuest (www.eduquest.net), and is available to subscribers of our GMP libraries.

Management responsibility is the cornerstone of any Quality System, according to the US Food and Drug Administration (FDA) and international quality standards.

The most sophisticated and compliant Quality System will not remain that way without vigorous and continuous management review and support. And unlike other duties, management cannot delegate its responsibility for quality.

US FDA does not expect management reviews to be just number-crunching exercises, such as tallying the number of open CAPAs or the amount of complaints. Instead, a management review should focus on what the quality data reveal about the overall health of the Quality System.

As a general rule, FDA will not request to see the results of a management review. However, FDA may want to confirm reviews actually take place and determine who attends them to ensure company procedures and schedules are being followed.

Here are the broad components of management reviews of the Quality System.

- Measurement: Reviews must measure a company's Quality System against FDA requirements and the company's own stated quality objectives as defined in its quality policy.
- Frequency: Management reviews must be conducted at defined intervals and with sufficient frequency. If there are too many quality issues not known or not addressed by executive-level management, reviews should occur more frequently.
- Documentation of procedures: Companies should have written procedures and schedules for doing the reviews. Companies also should document when reviews are held, along with their results.

Requirements commonly seen in management review procedures include a fixed agenda of topics to be discussed (with flexibility for unique agenda items to be added), the necessary attendees to participate in the management review, and how action items resulting from the review are to be addressed.

Management Reviews should ask and get answers to questions such as:

- Why are we having these problems?
- What are the root causes of our CAPAs and complaints?
- What parts of the Quality System are not working to our expectations?
- What parts require improvement?

MANAGEMENT REVIEWS: SAMPLE CHECKLIST *(Continued)*

An effective and compliant Quality System must include periodic management reviews held at defined intervals of sufficient frequency.

Management reviews should include assessments of your processes, products, and customer needs. In addition, they should focus on the overall health and effectiveness of your Quality System.

Note that the outcome of these management reviews typically includes improvements to the Quality System, improvements to products and manufacturing processes, and potential realignment of resources.

Here is a checklist of what management reviews should cover:

- Appropriateness of the quality policy and objectives.
- Results of audits and other assessments.
- Customer feedback (including complaints)
- Results of data trending analysis.
- Preventive action to avoid serious issues or recurrence of issues.
- Follow-up action from previous management reviews.
- Changes to business practices or environment.
- Ways product characteristics are (or are not) meeting customer needs
- Document and date the decisions and results coming out of your management reviews

UL Course: Management Responsibility for Quality: What FDA Expects (PHDV101)

Under FDA law and regulations, an effective and compliant Quality System literally begins and ends with management. This course explains who is considered management by FDA and management's responsibilities under FDA Good Manufacturing Practices.

Written by the experts at consulting firm EduQuest (www.eduquest.net), this course may be appropriate for managers and senior executives within Life Sciences organizations, to help them recognize how and why a successful Quality System depends on active management support and involvement to ensure safe and effective products reach patients and customers.

To preview the Management Responsibility course, contact Pat Thunell at pat.thunell@ul.com.

About UL Compliance to Performance

UL Compliance to Performance provides knowledge and expertise that empowers Life Sciences organizations globally to accelerate growth and move from compliance to performance. Our solutions help companies enter new markets, manage compliance, optimize quality and elevate performance by supporting processes at every stage of a company's evolution. UL provides a powerful combination of advisory solutions with a strong modular SaaS backbone that features ComplianceWire®, our award-winning learning and performance platform.

UL is a premier global independent safety science company that has championed progress for 120 years. It's more than 12,000 professionals are guided by the UL mission to promote safe working and living environments for all people.