What Makes An Effective CAPA Program

By Sarah Green

What does the FDA want to see when they review a manufacturing site’s Corrective Action Preventive Action (CAPA) program? What should an effective CAPA program look like? What resources are out there to help answer questions? I work in the radiopharmaceutical industry and my article covers what I’ve learned for pharmaceuticals. There are links at the bottom to more information for pharmaceuticals and medical devices.

Let’s start with a high-level summary then break it down. The FDA wants to see that there are procedures for handling a non-conformance once discovered, evaluating the risk to the patient, the amount of effort that went into the investigation, how the corrective action was implemented, and verification that the corrective action worked. On the preventive side, the FDA wants to see what is being done to prevent problems from occurring in the first place and that new controls in place prevent recurrences.

A non-conformance can be discovered from a variety of sources including a customer complaint, recall, audit, regulatory inspection, monitoring activities, deviations, product rejection, etc. It is always better to catch the non-conforming product before it is released. A detailed description of the problem should be written. Include details of how the problem was found and who discovered it. When the problem occurred and how often it has occurred. Be sure to document as much as possible as this shows the FDA the level of effort that was put in. Attach supporting documentation to prove the non-conformance exists such as a batch failure report. Be aware that the FDA should not, according to the Agency policy (CPG 7151.02), request records regarding results of internal quality audits, management reviews, third party audits (including ISO audits), or supplier audits. They will review the raw data that was audited and reviewed.

A Closed Loop Diagram is a great tool to help ensure that a CAPA is fully implemented. This shows the FDA that every step is thought through.

CAPA Management in a GMP Environment Life Science Technical Bulletin (February 2014)
After a non-conformance is discovered, the next step is to evaluate the impact that the problem could have on the patient. A Risk Assessment Tool Matrix can help determine if a CAPA investigation is necessary.

![Risk Assessment Tool Matrix](image)

Not every non-conformance requires a CAPA investigation. For example, if a technician forgets to initial a batch record. Re-training the employee would be sufficient. Per ICH Q9, Quality Risk Management, “The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.” During the evaluation process, assess and document the potential impact on product quality and safety to the patient that the non-conformity has on affected batch(es) and all released batch(es). If a CAPA investigation is deemed unnecessary, explain and document why. Also be sure to describe all remedial actions taken until the root cause is determined. Document deviations from Standard Operating Procedures (SOPs). If a CAPA investigation is necessary, assign a CAPA Index Number on a CAPA Tracking Log. The goal is to track the progress of the investigation. Assign a CAPA Owner, this person is responsible for directing the investigation activities.

During the investigation continue to collect as much documentation as possible and interview personnel who may have information. If possible, meet as a team to investigate and determine the root cause. It is helpful to have a diagram of the manufacturing process so that every step is examined. Document all meetings and describe what was discussed and outcomes. Explain all possible causes for the non-conformance and describe how each idea was tested. When the root cause is determined, explain how the team found the root cause. For medical devices, the FDA’s website has an example of a flow chart, see the link at the end of the article.

The corrective and preventive action is next implemented. Develop a plan listing the actions that need to be completed. Identify people responsible for each task and include timelines for when each task should be completed. Note any resources needed to complete tasks. List all SOPs that need to be modified. Describe in detail all process changes and evaluate whether the change needs to be approved by the FDA prior to implementing. Be sure to determine and document if the change in process could have an affect on the quality of the finished product. Review 21 CFR 314.70 to help determine if FDA approval prior to implementing is necessary.

After the corrective and preventive action is implemented the last step is to monitor and verify that the new or revised procedures and controls are effective. A good way to verify that the root cause was found and corrective actions successful is to remove the corrections and repeat the problem. Document that the corrective actions are implemented, controls are in place, monitoring activities continue, and
that there is no adverse effect on the finished product. Provide a CAPA report to management for their review.

On the preventive side, there are several activities a manufacturing facility can do to prevent problems from occurring. It is important to meet as a team and consider what could go wrong and think of ways to prevent those from happening. Document every meeting so that the FDA can see that steps have or are being taken to prevent problems. Trending data is effective in catching problems. Document monitoring activities. Record Key Performance Indicators. Follow established procedures such as handling incoming materials, maintaining equipment, training and re-training personnel, and facility maintenance. Review SOPs for accuracy and make any necessary changes. I’ve said this several times throughout, document everything. As the saying goes, if it isn’t documented it didn’t happen.

Here are some resources for developing and improving a CAPA program.


