HIERARCHY FOR CAPA EFFECTIVENESS

by Andy Barnett

Have you ever reviewed an investigation report and wondered whether the proposed corrective and preventive action (CAPA) would be effective?

Sometimes, we shrug our shoulders and say, "At least they put something in place". We all know that the FDA expects us to include an effectiveness check, but do we have enough guidance to make these checks meaningful? NSF suggests that you consider these three questions:

1. What will you measure?
2. When will you measure it?
3. What is your acceptance standard?

HERE ARE TWO EXAMPLES:

> Three months after implementation of the CAPA, check for repeat incidents. If there are no incidents, close the CAPA. If there are repeat incidents, re-open the investigation.

> Ten batches after implementation, calculate the new average reject rate. The CAPA is successful if the reject rate is less than 1.5 percent. If the new reject rate is higher than 1.5 percent, re-open the investigation.

But are these requirements sufficient? Is there any way we can evaluate the CAPA before implementation? We will lose valuable time if we must wait three to six months for the answer. The regulatory risk increases as the clock keeps ticking.

We propose introducing a CAPA hierarchy that investigators can use to help them select an appropriate corrective/preventive action that is most likely to deliver the desired outcome. It can also be used by approvers. It may even give them additional leverage to push back for a better solution, or perhaps

simply help them articulate the weaknesses they saw in previous CAPAs. After all, some corrective actions ARE more effective than others.

CAPA HIERARCHY

In order of *decreasing* effectiveness

1. Elimination
2. Replacement
3. Facilitation
4. Detection
5. Mitigation

ELIMINATION

Eliminate the ***possibility*** of error. This can be accomplished by eliminating the task. For example, eliminate mixing errors by purchasing pre-mixed materials. Eliminate recording errors by linking the measurement device to a printer.

Elimination can also be accomplished by a poka-yoke (an error-proof device). This concept is wide-spread in manufacturing where a special fixture makes a part impossible to install incorrectly.

For example, I participated in an investigation for IV bags that were shipped to the customer without a thermal print label. Every time the operator pushed

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the emergency stop button, the printer and camera would lose their memory, so the printer did not know what to print and the camera did not know what to reject. We eliminated the problem by revising the PLC program to automatically reject the in-process bags following an e-stop. We also added a verification clause to the validation procedure.

Use your imagination to think of other ways to adopt poka-yoke to pharmaceutical production.

REPLACEMENT

Change the current process by **replacing** it with one that is more reliable. Examples:

> Design a more robust screen for milling machines so they don't break so often.

> Add redundant sensors on machines so if one sensor fails, the other will still work and the process is still OK.

> Replace human inspection with 100-percent automated inspection at the source. Install bar-code scanners.

> Install mechanical limiting devices or PLC programs so that a process cannot exceed a specified range.

FACILITATION

Make the process easier to perform so that mistakes are less likely to occur. Examples:

> Use "visual factory" techniques such as 5S and color coding. Make errors more obvious.

> Redesign forms so they are easier to complete, and omissions are easy to spot.

> Use dedicated storage areas to reduce the possibility of material mix-ups.

> Reduce material handling. Every movement is an opportunity to make a mistake.

> Add pictures to procedures.

DETECTION

Improve detection by adding new or better sensors, at the source if possible. Examples:

> Add audible alarms or lights if a process is out of tolerance. Better yet, automatically shut down or add an interlock so the process cannot move to the next step.

> Use trending routines to signal before the process goes out of tolerance.

Understand that a corrective action that improves detection is inherently weaker than a corrective action that eliminates the problem. Why? Because detection does not prevent defects, it just prevents escapes. And defects cost you money!

MITIGATION

Minimize the effect of the error. This is typically the weakest form of corrective action. For most companies, product designs are constrained. Probably the only way to mitigate is to sort or rework, but this should be viewed as an interim step, not a permanent corrective action. This is true even if you design a perfect automated re-inspection system. Rework is a crutch.

Sometimes you can combine detection and mitigation. Examples:

> Install a metal detector with a link to the conveyor. When metal is detected, mitigate by stopping the conveyor before contaminating the bin.

> Use a camera to inspect fill volume and link it to a reject mechanism.

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CONCLUSION

Now that you aware of the CAPA hierarchy, I challenge you to consider reviewing a sample of past CAPA actions. How many fall into the detection and mitigation categories, which are the least effective actions you can take? I suspect that the percentages will surprise you.

Note that the CAPA hierarchy does not include retraining. Sometimes it is very difficult to find the root cause. Just be careful not to fall into the "blame and train" trap when you can't think of any alternative actions. Training is necessary, but not sufficient. What happens in six months when there is employee turnover? People are human, and people make mistakes. If training is one of the CAPA actions, just be sure to supplement it with at least one additional CAPA that falls into the CAPA hierarchy categories listed in this article.

Roll out the CAPA hierarchy to your organization and you will have a better chance of implementing preventive actions that deliver significant improvements. With the CAPA hierarchy, you can anticipate an effective outcome, rather than waiting several months for the CAPA implementation, only to be disappointed by the results of the effectiveness check.

If you have any questions or require assistance, don't hesitate to contact us at **USpharma@nsf.org** or **pharmamail@nsf.org**.

To watch NSF's latest video on the CAPA hierarchy by Jim Morris, visit our resource library – **www.nsf.org/info/pblibrary**

ABOUT THE AUTHOR

For over 20 years, Andy Barnett has worked with clients in the pharmaceutical, medical device, biologic and biotechnology industries to develop quality assurance and regulatory strategies for compliance with U.S. FDA regulations. His particular expertise includes providing statistical support for process development, process characterization and optimization; assisting with remediation activities, especially corrective actions and process improvement; and providing training in root cause, corrective actions and statistical methods for process improvement.

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