Methods of root cause package failure analysis

Overview

Package integrity is critical in maintaining product sterility. The infection rates in hospitals continue to soar and the number of fatalities associated with infections cannot be ignored. It is with this knowledge that we continue to strive for reliable sterile barrier packaging.

The reasons for packaging failures must be understood and addressed. In sterile barrier packaging, integrity is everything.

The basis for package failure analysis is not new. It encompasses the four basic principles of problem solving: define the problem, identify the root cause, implement an action plan, and evaluate the results. Problem solving is a skill that can be learned and requires practice. It has individual styles and approaches. Effective problem solving requires thinking about the "big picture" and should involve a multifunctional team.

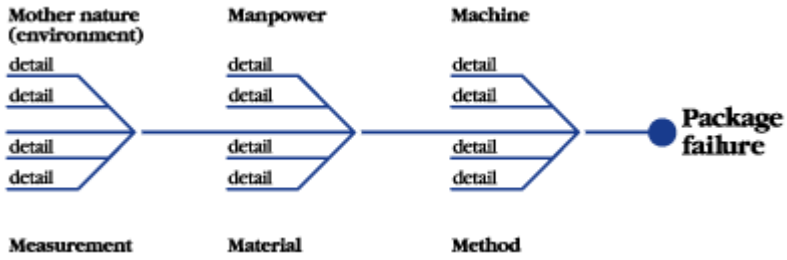
This paper will discuss methods for identifying a problem's root cause; anomalies that can cause seal failures; and what to look for when choosing a packaging supplier.

Methods of identifying the root cause

There are many different problem solving methods to choose from, such as "The Five (5) Whys", "Fishbone Analysis", "Is/Is Not" and many others. What's important is that you choose the one that your team is most comfortable with. It will help build the team's commitment through equal participation in the process. Use combinations of techniques and assign action items and due dates. The more questions you ask, the sooner you will arrive at the true root cause or causes. Finally, generate your hypothesis and when possible recreate the anomaly to prove your theory. Should your theory prove to be correct, implement corrective and preventive action and follow-up with an effectiveness check.

Fishbone Analysis (also known as the "Ishikawa Diagram")

Fishbone analysis allows the team to identify, explore, and graphically display, in detail, all of the possible causes related to a problem or condition to discover its root cause(s). The fishbone visually represents the many possible causes for a problem.



This problem solving method enables the team to focus on the content of the problem, not on the history of the problems or differing personal interests of team members and creates a snapshot of the collective knowledge and consensus of the team around a problem. In turn, this builds support for the resulting solutions and focuses the team on the causes, not symptoms.

When using fishbone analysis, draw a line across the page attached to a problem statement, and several lines or 'bones' coming from the main line. Each line can be labeled with one of the "6 Ms": machine, manpower, material, measurement, method, and mother nature (environment). The team can then brainstorm possible causes and include them on the appropriate 'bones.'

Once the fishbone has been completed, the team can prioritize the root causes they have identified.

Five Why

Toyota's Five-Why method is straightforward, asking why the problem occurred, and why that cause is causing problems. Once you ask "why" an adequate number of times (not always five!), you will have found the root cause. It doesn't include breaking down the date, regression analysis or other advanced statistical tools.

To employ the Five-Why technique:

1. Write down the specific problem. Writing the issue helps you formalize the problem and describe it completely. It also helps a team focus on the same problem.
2. Ask why the problem happens and write the answer down below the problem.
3. If the answer you just provided doesn't identify the root cause of the problem, ask 'why' again and write that answer down.
4. Loop back to step 3 until the team is in agreement that the problem's root cause is identified. This may require asking 'why' less than or more than five times.

The object is to quickly reach through the layers of issues and lead to the root cause.

Is/Is Not

This problem-solving technique helps the team document the what, when, where, and how big of a problem. It also helps in determining the scope of a solution and what that solution will or will not address, thereby keeping the team focused and protecting against project or scope "creep".

What to do next

Use a combination of techniques if necessary, and assign action items and due dates. Keep in mind that there may be more than one cause for any given problem. The more questions you ask, the faster you'll come to the true root cause or causes.

Once you've identified a cause, generate a hypothesis and, if possible, recreate the anomaly to prove your theory. If the theory is correct, implement corrective and preventative action (CAPA) and follow that up with an effectiveness check. If it's not, begin where you left off and continue your problem solving efforts using the information gained from testing the theory.

Anomalies that can cause seal failures

	Wrinkles or creases in substrates	Contamination of substrates, silicone transfer from tray	Missing adhesive or lack of adhesive	Lack of compatibility of adhesive to substrate	Stainliber creep	Defects in component substrate	Warped lid, won't lie flat on tray	Product too large for pouch, example: wrinkles at fourth and final seal	Incorrect or uneven tension in processing equipment	Damaged heat seal platen	Incorrect peeling technique	Die rubber (damaged, cut or degraded, incorrect durometer)	Sealing parameters (temp, dwell, pressure)	Bent or folded trays, lids or pouches	Incorrect formulation in adhesive or substrate material	Dirty processing rollers, calendaring, contact, nip, etc	Thin locations in substrate	Component stock not compatible with device (size, weight, orientation)	Film applied to incorrect side of component (wire vs lid)	Contaminated adhesive	Incorrect component	Edge weave while processing roll stock	Incorrect die platen size, measurement	Out of calibration	Gage R&R unacceptable	Incorrect test method (ie 180° supported vs 90° unsupported)	Test method not validated
Channels into or through Seal	X	X	X	X	X	X		X	X	X		X	X	X					X									
Wrinkles in Substrate, Pouch or Lid	X						X	X	X					X				X	X									
Poor Seal Transfer		X	X	X		X				X	X	X	X	X	X			X		X	X	X			X			
Low Peel or Burst Value		X	X	X	X					X	X	X	X	X	X				X	X	X	X	X	X	X	X	X	X
Integrity Test Failure, Bubble or Leak Test	X	X	X	X	X	X		X	X	X			X	X	X				X	X	X	X	X	X	X	X		X
Seal Width too Narrow					X					X		X											X	X				
Failing DSC or IR Testing		X													X						X	X			X	X		X
Incomplete Seal	X	X	X	X	X	X		X		X		X	X	X	X					X	X	X			X	X		X
Holes in Substrate						X		X						X		X	X	X										
Delamination/Fiber Tears				X		X					X	X	X		X		X		X	X	X	X						
Test Equipment/Method			X																						X	X	X	X

(Click on chart to enlarge)

Choosing the right packaging supplier

Ultimately, it is up to the device or pharmaceutical manufacturer to ensure that their packages are providing an adequate sterile barrier thereby contributing to the release of a safe and effective product; however, there are several things one should expect from one's packaging supplier.

Honesty and integrity are a must and cannot be substituted at any cost. Suppliers should come to the table understanding that they are making packaging for use in sterile barrier applications and that **patient safety is of the highest concern and is not negotiable**. GMP compliance is a must; a supplier's system should mirror the MDM's. A robust CAPA system is critical and should include the entire gamut of corrective action requirements: correction, corrective action, preventive action, containment action, remedial action, and the verification of effectiveness. Compliance to the newly revised ISO 11607:2006, parts 1 and 2, is the standard to which MDMs are—and therefore

suppliers should be—held. Solid validation work encompassing multiple lots, worst case scenarios, and the IQ/OQ/PQ format should be the norm.

Customers should be allowed to actively participate in the validation efforts, as again, they are ultimately responsible for the safety and effectiveness of their devices. Open lines of communication and an understanding of the MDM's packaging needs will help to ensure that the correct packaging is chosen for each application. Suppliers should be **willing to listen and should understand the regulatory risk** your company is ensuing when using their packaging. And finally, principle personnel should have a demonstrated background in the medical device or pharmaceutical arena to better suit your needs.

Conclusion

The regulatory climate continues to push effectively defined and established quality systems down to the lower tiers or suppliers and subcontractors. The days of being able to assume your supplier is providing you with a safe and effective package are fast fading. Today's MDMs are requiring proof of an effective quality system and expect a demonstrated record of service, responsiveness and quality. It is the only way that we can ensure that our packaging is truly providing an adequate sterile barrier.

References

ISO 11607:2006 Packaging for Terminally Sterilized Medical Devices—Part 1: Requirements for Materials, Sterile Barrier Systems, and Packaging Systems and Part 2: Validation Requirements for Forming, Sealing, and Assembly Processes are available for purchase from AAMI at www.aami.org

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About the author

Lora Keena is Oliver Medical's director of QA/RA and oversees inspection and compliance for Oliver's US and European facilities. She has presented this white paper at many medical device manufacturing industry conferences.