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Management of CAPA
&
Case Studies

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Purpose

To describe the procedure for initiating, approving, implementing, closing out and monitoring effectiveness of Corrective and Preventive Action (CAPA) which are generated through quality management system.

References

- ICH Q7: Good Manufacturing Practice for Active Pharmaceutical Ingredient.
- ICH Q9: Quality Risk Management
- ICH Q10: Pharmaceutical Quality System.
- EU guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use
- Title 21 Code of Federal Regulations Parts 210 and 211

References

ICH Q10: Pharmaceutical Quality System.

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3.2.2 Corrective Action and Preventive Action (CAPA) System

The pharmaceutical company should have a system for implementing corrective actions and preventive actions resulting from the investigation of complaints, product rejections, non-conformances, recalls, deviations, audits, regulatory inspections and findings, and trends from process performance and product quality monitoring. A structured approach to the investigation process should be used with the objective of determining the root cause. The level of effort, formality, and documentation of the investigation should be commensurate with the level of risk, in line with ICH Q9. CAPA methodology should result in product and process improvements and enhanced product and process understanding.

Reference

ICH Q10: Pharmaceutical Quality System.

Corrective Action:

Action to eliminate the cause of a detected non-conformity or other undesirable situation. NOTE: Corrective action is taken to prevent recurrence whereas preventive action is taken to prevent occurrence. (ISO 9000:2005)

Preventive Action:

Action to eliminate the cause of a potential non-conformity or other undesirable potential situation. NOTE: Preventive action is taken to prevent occurrence whereas corrective action is taken to prevent recurrence. (ISO 9000:2005)

Reference

ICH Q10: Pharmaceutical Quality System.

Table II: Application of Corrective Action and Preventive Action System throughout the Product Lifecycle

Pharmaceutical Development	Technology Transfer	Commercial Manufacturing	Product Discontinuation
Product or process variability is explored. CAPA methodology is useful where corrective actions and preventive actions are incorporated into the iterative design and development process.	CAPA can be used as an effective system for feedback, feedforward and continual improvement.	CAPA should be used and the effectiveness of the actions should be evaluated.	CAPA should continue after the product is discontinued. The impact on product remaining on the market should be considered as well as other products which might be impacted.

Reference

ICH Q9: Quality Risk Management

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2. SCOPE

This guideline provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).

3. PRINCIPLES OF QUALITY RISK MANAGEMENT

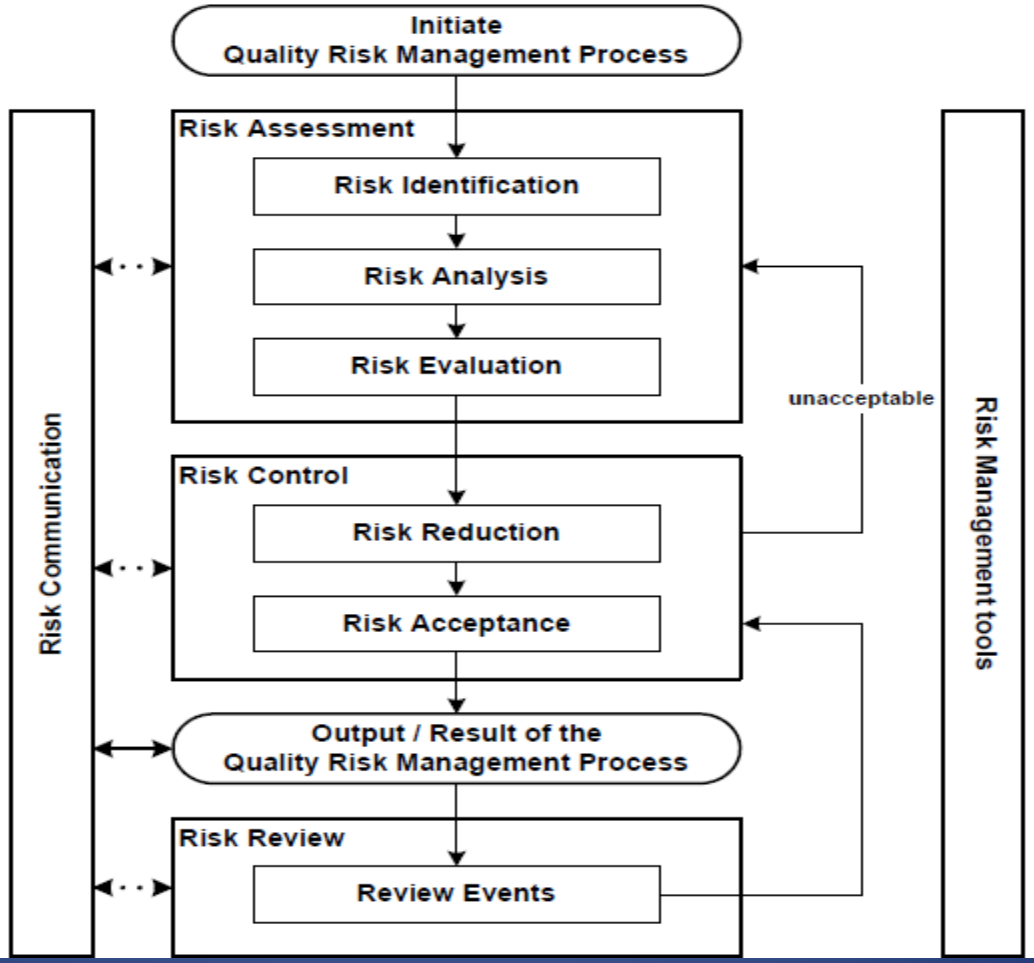
Two primary principles of quality risk management are:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
- The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.

Reference

ICH Q9: Quality Risk Management

Figure 1: Overview of a typical quality risk management process



Reference

ICH Q9: Quality Risk Management

Risk identification is a systematic use of information to identify hazards referring to the risk question or problem description. Information can include historical data, theoretical analysis, informed opinions, and the concerns of stakeholders. Risk identification addresses the "What might go wrong?" question, including identifying the possible consequences. This provides the basis for further steps in the quality risk management process.

Risk analysis is the estimation of the risk associated with the identified hazards. It is the qualitative or quantitative process of linking the likelihood of occurrence and severity of harms. In some risk management tools, the ability to detect the harm (detectability) also factors in the estimation of risk.

Risk evaluation compares the identified and analyzed risk against given risk criteria. Risk evaluations consider the strength of evidence for all three of the fundamental questions.

Reference

ICH Q9: Quality Risk Management

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Risk reduction focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level (see Fig. 1). Risk reduction might include actions taken to mitigate the severity and probability of harm. Processes that improve the detectability of hazards and quality risks might also be used as part of a risk control strategy. The implementation of risk reduction measures can introduce new risks into the system or increase the significance of other existing risks. Hence, it might be appropriate to revisit the risk assessment to identify and evaluate any possible change in risk after implementing a risk reduction process.

Risk acceptance is a decision to accept risk. Risk acceptance can be a formal decision to accept the residual risk or it can be a passive decision in which residual risks are not specified. For some types of harms, even the best quality risk management practices might not entirely eliminate risk. In these circumstances, it might be agreed that an appropriate quality risk management strategy has been applied and that quality risk is reduced to a specified (acceptable) level. This (specified) acceptable level will depend on many parameters and should be decided on a case-by-case basis

Reference

ICH Q9: Quality Risk Management

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Additionally, the pharmaceutical industry and regulators can assess and manage risk using recognized risk management tools and/ or internal procedures (e.g., standard operating procedures). Below is a non-exhaustive list of some of these tools (further details in Annex 1 and chapter 8):

- Basic risk management facilitation methods (flowcharts, check sheets etc.);
- Failure Mode Effects Analysis (FMEA);
- Failure Mode, Effects and Criticality Analysis (FMECA);
- Fault Tree Analysis (FTA);
- Hazard Analysis and Critical Control Points (HACCP);
- Hazard Operability Analysis (HAZOP);
- Preliminary Hazard Analysis (PHA);
- Risk ranking and filtering;
- Supporting statistical tools.

Scope

This procedure is applicable to corrective and preventive actions implemented at all manufacturing facilities and supporting functions

Responsibility

CAPA Originator

- Request and get the CAPA form issued by QA.
- Document the CAPA plan and submit to CAPA owner.
- Execute CAPA as directed by Head of the Department

CAPA Owner (Head of affected department)

- Review the CAPA plan & propose additional inputs, if required.
- Submit the CAPA to Head-QA / designee for review and approval
- Ensure implementation of CAPA plan after Head-QA approval

Responsibility

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Head-QA / Designee

- Review and Approve the CAPA plan
- Provide technical or regulatory input to the CAPA plan, as applicable
- Consult Site Quality Head for final decision and approval, if CAPA plan is not satisfactory

Quality Assurance

- Assign number and log the CAPA. Issue CAPA form.
- Keep track of completion and closure of CAPA
- Verify CAPA records along with supporting documents for completeness and effectiveness.
- Archival of CAPA reports.

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Responsibility

Plant Head

- Review and approve CAPA. Review and approve Effectiveness check initiated for Implemented CAPA.
- Provide recommendation in CAPA and / or Effectiveness Check, if required.

Head of other departments

- Execute CAPA relevant to department, if identified.
- Maintain state of compliance in respective department.

Site Head Quality

- Final Closure of CAPA .
- Review and approve Effectiveness check initiated for implemented CAPA .

Accountability

Site Head-Quality is accountable for implementation of the SOP.

Definitions

Correction

Correction refers to immediate action taken to repair, rework or adjustment and relates to the disposition of an existing non-conformity.

Corrective Action

Action taken to eliminate the cause of an existing non conformity, defect or other undesirable situation in order to prevent recurrence.

Deviation

Deviation is either an unexpected event or result associated with a GMP related activity. It includes events or results deviating from established standards, procedures, processes, protocols, specifications, and registered details. Departure of an activity from its documented standard operating procedures.

Definitions

Function

Section of a department, or department where activity has occurred / will occur.

Non-conformity

When a product, process, procedure, system, or structure deviates from quality management system requirements, a formal nonconformity exists.

Preventive Action

Action taken to eliminate the cause of a potential nonconformity, defect, or other undesirable situation in order to prevent occurrence.

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Definitions

CAPA originator

Representative from the department where from the root cause/ most probable cause is to be eliminated. This person shall be identified by Head of the department.

CAPA Owner

Head of the department where from the root cause/ most probable cause is to be eliminated.

Corrective and Preventive Action (CAPA)

A systematic approach which includes actions needed to correct ("Correction"); prevent recurrence ("Corrective action") and eliminate the cause of potential ("Preventive action") non-confirming product and other quality problems.

Procedure

- **General**
- Review and Refer to the event such as Incident, deviation, OOS, Product Complaint, Product Failure, Product Recall etc. and corresponding root cause / probable cause identified through investigation of the event.
- Immediate actions / corrections taken before proposing CAPA also shall be noted and documented.
- CAPA proposed shall be appropriate to the root cause / most probable cause.

Procedure

- Corrective Actions as well as Preventive Actions are the ways to mitigate risk to the product, process, equipment or facilities. In order to develop the proper Corrective Actions and Preventive Actions (CAPA) system it is desirable that risk associated to the process, product, equipment or facilities are understood and Appropriate actions are initiated.
- Reference to the CAPA shall be documented in all relevant forms.
- Corrective Actions and Preventive Actions (CAPA) shall be applied throughout the life cycle time of the product.

Procedure

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- **Steps involved in CAPA procedure**

- Events triggering CAPA
- Issuance and logging of CAPA
- Proposal of CAPA Plan by Originator
- Review of CAPA plan by CAPA owner (Head of affected department)
- Approval of CAPA plan by Plant Head and Head-QA

Procedure

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- **Steps involved in CAPA procedure**

- Communication of CAPA plan
- Extension Request for CAPA
- Verification of CAPA by QA
- Closure of CAPA by Head QA and Site Head Quality
- Trending of CAPA and Effectiveness Check by QA
- Flow chart CAPA process

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

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PROBLEM DEFINITION-

Air Florida Flight 90 was a scheduled U.S. domestic passenger flight operated by on January 13, 1982, the Boeing 737-200 crashed into the 14th Street Bridge over the Potomac River just two miles from the White House.

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

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SUMMARY INVESTIGATION & ROOT CAUSE-

The National Transportation Safety Board (NTSB) determined that the **cause of the accident was pilot error.**

- ✓ The **pilots failed** to switch on the **engines' internal ice protection system,**
- ✓ **used reverse thrust** in a snowstorm prior to takeoff,
- ✓ tried to use the **jet exhaust of a plane in front** of them to melt their own ice, and
- ✓ **failed to abort the takeoff** even after detecting a power problem while taxiing and visually identifying ice and snow buildup on the wings.

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FLIGHT 90- POTOMAC RIVER CRASH

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INVESTIGATION-

The investigation of the crash concluded that the combination of the crew's use of thrust reverse on the ground, and their failure to active the engine anti-ice system, caused the crash.

By **failing to activate the engine anti-ice,** the large amounts of snow and ice that were sucked into the engines during reverse thrust use was allowed to remain there, unchallenged.

The ice buildup on the compressor inlet pressure probe, **the probe which measures engine power, can cause false readings**, as was the case here. The indications in the cockpit showed an **Engine Pressure Ratio of 2.04**, while the power plants were in reality only producing 1.70 EPR, or about 70% of available power.

The combination of the **ice covered wings and low power caused an immediate stall** on takeoff that resulted in 74 lives lost.

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FLIGHT 90- POTOMAC RIVER CRASH

INVESTIGATION-

While running through the takeoff checklist, the following conversation took place:

CAM-2: Air conditioning and pressurization?

CAM-1: Set.

CAM-2: Engine anti-ice?

CAM-1: OFF

When the Cockpit Voice Recorder tape was played back after recovery, there was much disagreement about Capt. **Wheaton's response to "anti-ice."**

Many of the investigators could not accept the fact that, despite the freezing 20 degree temperatures and 25+ inches of snow on the ground, Wheaton said "off."

The tapes were taken to the FBI Labs in Washington for analysis, and it was concluded that the word was, in fact, "off**." Apparently, despite the weather, the crew had forgotten to activate the anti-ice systems.**

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INVESTIGATION-

At 3:59 pm, 'Palm 90' was cleared for takeoff with the remark "no delay on departure, if you will, traffic's two and a half out for the runway," added a few seconds later by ATC. Pettit advanced the throttles, and quickly responded "real cold, real cold," implying that the engines reached the takeoff EPR of 2.04 before the throttles had been fully advanced.

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FLIGHT 90- POTOMAC RIVER CRASH

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INVESTIGATION-

Throughout the entire takeoff roll, the First Officer tried to inform the Captain that something wasn't right, but it was in vain. Wheaton was sure everything was in order:

15:59:51 CAM-1 It's spooled. Real cold, real cold.
15:59:58 CAM-2 God, look at that thing. That don't seem right, does it? Uh, that's not right.
16:00:09 CAM-1 Yes it is, there's eighty.
16:00:10 CAM-2 Naw, I don't think that's right. Ah, maybe it is.
16:00:21 CAM-1 Hundred and twenty.
16:00:23 CAM-2 I don't know.
16:00:31 CAM-1 Vee-one. Easy, vee-two.

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

INVESTIGATION-

At rotation speed, the aircraft pitched up sharply, causing Wheaton to reply "easy."

It was a known fact that ice buildup on the wings of a 737 can cause a tendency to pitch up. Pettit's correction of the nose-up attitude, however, failed to resolve the problem and the stick shaker immediately began to sound. Wheaton called "Forward, forward, easy. We only want 500," referring to the altitude at which the airplane had to be to make the 40 degree turn to the left around the Washington Monument and the restricted airspace over the Capitol. "Come on. Forward, forward. Just barely climb," exclaimed Wheaton as the aircraft continued to stall. ***Moments later the aircraft was no longer climbing, but falling back to earth.***

"Stalling, we're falling."

"Larry, we're going down Larry."

"I know it."

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

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Root Cause…News Report…

After rolling 3,500 feet, the point where the twin-engine jet should have been airborne, Petit expressed concern about the plane's lack of power.

According to the cockpit voice recorder, he said, "**God, look at that thing," referring to an engine power gauge. "That don't seem right, does it?“**

"Yes it is," said Wheaton, the captain.

"Naw, I don't think that's right," Petit said. "Maybe it is. I don't know."

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

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ROOT CAUSE… News Report…

Because they neglected to use the engine anti-ice device, ***they were getting erroneous readings on their engine gauges.***

As a result, they had set their power to ***only 80 percent*** of what was needed for a successful takeoff.

Ironically, ***federal investigators*** would later say, the 737's Pratt & Whitney engines had plenty of reserve power. All the pilots had to do was advance the throttles to draw on it.

But they didn't, most likely because their judgment was clouded by stress.

The plane limped into the air and almost immediately lost airspeed as its nose pitched up. It began to vibrate violently.

"Stalling," one of the pilots yelled. "We're stalling."

Then, Petit cried out, "Larry, we're going down. Larry!"

An apparently resigned Wheaton responded, "I know it."

Acts of heroism

CASE STUDY –1

FLIGHT 90- POTOMAC RIVER CRASH

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CORRECTION

Not done, all 74 passengers including crew is killed

CA & PA

Regulatory and procedure changes

The investigation following the crash, especially regarding the ***failure of the pilot to respond to crew concerns about the deicing procedure***, it became a widely used case study for both air crews and rescue workers.[

- ✓ led to a number of reforms in ***pilot training*** regulations.
- ✓ Partial blame was placed on the ***young, inexperienced flight crew***,
- ✓ Another result of the accident was the development of an ***improved rescue harness*** for use in helicopter recoveries.
- ✓ After the crash, airlines began enacting policies to ensure that at ***least one older, more seasoned crew member*** was on board planes at all times.
- ✓ They also began reappraising the traditional unwritten rule that the ***captain had ultimate authority*** on a flight and could not be questioned. From that point onward, ***first officers were encouraged to speak up if they believed a captain was making a mistake.***

CASE STUDY – 1

FLIGHT 90- POTOMAC RIVER CRASH

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Impact and Results-

Contribution to demise of Air Florida

"The Air Florida accident led to the carrier's eventual demise. Though it was once a robust airline, flying to 30 cities through Florida, the Northeast and the Caribbean, the company filed for bankruptcy and grounded its fleet in July 1984

Flight 90: TV Movie

Disaster on the Potomac is a true story based on the crash of Air Florida flight 90 on January 13, 1982 in Washington D.C. This movie follows the main players throughout the day,...

More details at….

https://en.wikipedia.org/wiki/Air_Florida_Flight_90

https://web.archive.org/web/20150612074913/http://www.airdisaster.com/special/special-af90.shtml

CASE STUDY – 2

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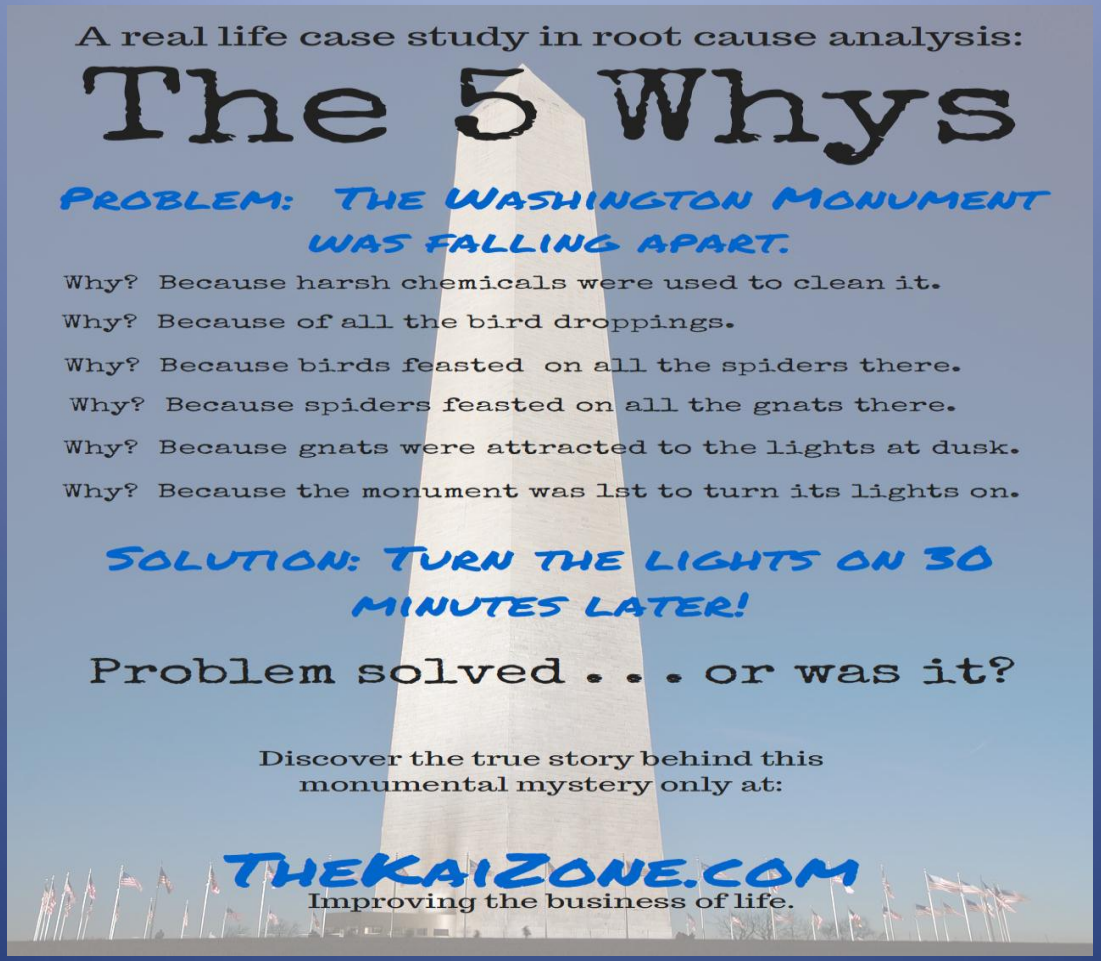
5 Whys Folklore: The Truth Behind a Monumental Mystery



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5 Whys Folklore: The Truth Behind a Monumental Mystery

Problem Definition:

One of the monuments in Washington D.C. is deteriorating.

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5 Whys Folklore: The Truth Behind a Monumental Mystery

SUMMARY INVESTIGATION & ROOT CAUSE:

Change how the monument is illuminated in the evening to prevent attraction of swarming insects.

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5 Whys Folklore: The Truth Behind a Monumental Mystery

INVESTIGATION-

The 5- Whys is a method of root cause analysis in which the learner repeatedly asks, “why?” in order to drill down from higher-level symptoms to the underlying root cause(s) of a problem. So critical is this line of logic to lean thinking that Taiichi Ohno once described the method as -

“the basis of Toyota’s scientific approach . . . by repeating why five times, the nature of the problem as well as its solution becomes clear.”

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5 Whys Folklore: The Truth Behind a Monumental Mystery

INVESTIGATION-

Why #1 – Why is the monument deteriorating?

- Because harsh chemicals are frequently used to clean the monument.

Why #2 – Why are harsh chemicals needed?

- To clean off the large number of bird droppings on the monument.

Why #3 – Why are there a large number of bird droppings on the monument?

- Because the large population of spiders in and around the monument are a food source to the local birds

Why #4 – Why is there a large population of spiders in and around the monument?

- Because vast swarms of insects, on which the spiders feed, are drawn to the monument at dusk.

Why #5 – Why are swarms of insects drawn to the monument at dusk?

- Because the lighting of the monument in the evening attracts the local insects.

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INVESTIGATION-

As detailed in an article from the ***Associated Press in 1989***, a group of private consultants were hired by the National Park Service (to the tune of $2 million) to perform a year-long study of the deterioration of the Lincoln Memorial and the Jefferson Memorial.

CASE STUDY – 2

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5 Whys Folklore: The Truth Behind a Monumental Mystery

Root Cause Report -

Myth #1 – Whose Monument is it, Anyway?

The first bit of mystery surrounding the tale is the exact monument that was experiencing the deterioration. Some versions specify the Washington Monument, some the Lincoln Memorial and others the Jefferson Memorial.

In April of 1990, the consultants published a report which found that –

- ✓ "the increasingly toxic effects of nature" had accelerated the erosion of the monuments and that immediate steps were required to address "very serious structural problems".

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Root Cause Report -

Myth #1 – Whose Monument is it, Anyway?

. A Park Service representative responded to the findings by assuring that “both memorials are in excellent shape overall” and that there was “absolutely no danger to the public”. Less than one month later in May of 1990, a 50 lb. block of marble fell from the volute on the top of a column in the Jefferson memorial.

P.S. Thankfully, no one was injured, and major repair and rehabilitation projects were subsequently initiated to address the deficiencies in both monuments.

CASE STUDY – 2

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Root Cause Report -

Myth #2 – Cleaning Chemicals as the Culprit

In most versions of the story, the erosion and degradation of the monuments were attributed to the ***use of the harsh chemicals*** needed to remove the bird droppings from the monument's surfaces. This explanation falls short of the complete truth in two ways.

First, the ***act of cleaning*** was cited only as one contributing factor among many

- like acid rain,
- water seepage,
- air pollution and
- littering tourists – to the damage observed on the memorials.

Second, cleaning chemicals were not causing the lion's share of the deterioration. Rather, ***per the consultants report***, it was actually the ***large volume of water*** applied during the cleaning process that was found to pose the greatest threat to the marble and limestone buildings.

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CORRECTION & CAPA Report –

Myth #2 – Cleaning Chemicals as the Culprit

Although ***very little could be done to reduce the volume of exterior rainwater*** to which the memorials were exposed, measures focused on reducing the volume of water used internally within the monuments as part of the cleaning process.

The Associated Press Article from 1990 stated that the Park Service had “dramatically reduced the volume of water used to wash the monuments”,

….***even going so far to say that they would need to “educate the public to understand that these buildings may not appear as pristine white in the future as they once did” because of the reduction in water used to clean them.***

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INVESTIGATION -

Myth #3 – Cleaning was for the Birds

Don Messermith is an esteemed professor emeritus at the University of Maryland. His accomplishments in the field of entomology – the scientific study of insects – are many, as evidenced by the extensive list of distinguished titles, prestigious awards, and publications that bear his name. But among his comprehensive catalog of contributions, one study in particular stands out above the rest.

It is true, the large prevalence of bird droppings – specifically from starlings and sparrows – did contribute to the need for a daily scrubbing of both monuments.

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5 Whys Folklore: The Truth Behind a Monumental Mystery

CORRECTION & CAPA Report –

Myth #3 – Cleaning was for the Birds

However, the bulk of the mess was not cause by a bird byproduct. As the story goes, Midgets (not Gnats) swarmed to the river-side monuments because the lights replicated their preferred, dusky mating conditions.

Rather than doing the deed over the water, the lights drew them inland in vast swarms where they splattered against the monument walls to deposit their eggs in the form of dark – not to mention hard-to-clean – masses.

Although the prevalence insects did invite a large population of spiders, which in turn brought the starlings and sparrows, it was the midges themselves that necessitated the bulk of the bathing.

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5 Whys Folklore: The Truth Behind a Monumental Mystery

CORRECTION & CAPA Report –

Myth #3 – Cleaning was for the Birds

Change how the monument is illuminated in the evening to prevent attraction of swarming insects.

CASE STUDY – 2

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5 Whys Folklore: The Truth Behind a Monumental Mystery

The Moral of the Story

Like all good stories, there is much to be learned from the tale of the Lincoln and Jefferson memorials. But without knowing the whole story, it's difficult to say exactly what the most important lesson is.

Maybe it's the value that a thorough understanding of cause and effect has on the efficiency and effectiveness of solutions.

Maybe it's the difficulty of solving complex problems under real world conditions. Perhaps, however, it's the importance of hope. Yes . . . *hope*. Because if these recent images of the Lincoln Memorial and the Jefferson Memorial at sunset are any indication, than there might just be hope yet.

More details at….

http://thekaizone.com/2014/08/5-whys-folklore-the-truth-behind-a-monumental-mystery/

Messersmith, Donald H. 1993. ***Lincoln Memorial Lighting and Midge Study****. Unpublished report prepared for the National Park Service. CX-2000-1-0014. N.p*

https://en.wikipedia.org/wiki/Air_Florida_Flight_90

CASE STUDY – 2

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5 Whys Folklore: The Truth Behind a Monumental Mystery

CASE STUDIES
Out of Specification results

CASE STUDY – OOS 1

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Problem definition:

Out of specification results (on higher side of the specification) observed during finished stage for Solid dosage form (Tablet) for assay test, however result of semi-finished (bulk) was within specification limit.

Observed value: 108.4% (Limit: 95.0% to 105.0%)

Investigation Details:

Phase I (Preliminary Lab investigation)

- ✓ Raw data was verified and found that the analyst had done the reporting as per test procedure.
- ✓ During interaction with analyst no root cause was identified.
- ✓ Bench top solution and volumetric flask was also found satisfactory.
- ✓ Calibration and PM status of instrument was also found within validity period.

CASE STUDY – OOS 1

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Investigation Details:

Phase I (Preliminary Lab investigation)

- ✓ During investigative testing, Instrument error, Sample preparation error (dilution error, extraction error and filtration error) had been ruled out.
- ✓ Chromatographic pattern was reviewed with respect to historical trend and found that a placebo peak was always closely eluted with the active content peak in sample chromatograms.
- ✓ *However this type of chromatographic pattern was not observed during original analysis and investigative analysis.*
- ✓ Based on this observation it was suspected that ***placebo (excipient) peak might be co-eluted (Merge) with active content peak which is leading higher results.***

CASE STUDY – OOS 1

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Investigation Details:

Phase I (Preliminary Lab investigation)

- Further pH of mobile phase was verified .It was suspected that ***analyst might have missed to mix the mobile phase*** after addition of buffers.
- As an investigation mobile phase has been freshly prepared (with proper mixing after addition of the buffers) and pH of final solution was compared with respect to original mobile phase and found that there is variation in pH within these two mobile phase, which confirms that ***there was a mobile phase preparation error.***
- Same investigative set has been re-run with freshly prepared mobile phase and elution pattern found as per historical trend i.e. both the peaks got separated and results were found within the specification limit.
- ***Retest has been performed and results found comply with specification.***

CASE STUDY – OOS 1

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CAPA:

- SOP on Good chromatographic practice has been revised to introduce Second check for the critical check parameters.
- This OOS was discussed with the analysts and importance of mixing of the solution after addition of the buffers phase was specifically stressed.
- Original analysis had been invalidated and retest results are considered for reporting.

Impact assessment:

As an impact assessment data of all the batches of this product was reviewed for the chromatographic pattern & found satisfactory.

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CASE STUDY – OOS 2

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Problem definition:

OOS observed for preservative content test in one of the Injection product.

Investigation Details:

Phase I (Preliminary Lab investigation)

No laboratory error was identified during Preliminary laboratory investigation.

Phase-II (Shop floor Investigation)

During Phase-II (Shop floor) investigation it was noticed that dispensing of preservative was done with ***inadequate selection of balance.*** Required accuracy was not achieved during dispensing. i.e. ***30 Kg balance was used with least count of 0.001 Kg for weighing of 25g*** material. Due to this; Extra quantity of preservative might got dispensed & remained unidentified due to less accuracy of balance.

CASE STUDY – OOS 2

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CAPA:

- ✓ This OOS was discussed with staff members and training has been imparted to address importance of selection of weighing balance for dispensing of material.
- ✓ Operating range for each balance has been displayed prominently.

Impact assessment:

As an Impact assessment data of all the batches manufactured by using the same type of balance was reviewed & found within the acceptance criteria.

The subject batch was rejected

CASE STUDIES
Deviation Results

CASE STUDY – DEVIATION 1

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Deviation: Departure from the established procedure/process.

Brief description:

Analyst has run the sequence with ***single injection*** of sample solution instead of duplicate as mentioned in respective testing procedure.

Investigation & Impact Assessment:

- ✓ As per testing procedure sample solution to be injected in duplicate.
- ✓ This has been identified by the analyst during calculation. Hence deviation has been logged & new sequence has been prepared on HPLC system with duplicate Injection of sample solution. (Protocol Bound retesting done)
- ✓ The calculation has been performed for both the set, with single Injection as well as for duplicate injection. The obtained results were comparable.

CASE STUDY – DEVIATION 1

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Root cause:

Based on the above investigation it is concluded that the above error has been occurred due to oversight of procedural requirement by involved analyst.

CAPA:

- ✓ Awareness training imparted to the group of analyst.
- ✓ Second person check has been introduced for the critical steps during analysis.

CASE STUDIES
Audit Observation

CASE STUDY – Audit Observation:

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Problem definition-

GMP documents were found in waste bin/ destruction box.

Investigation & Root Cause:

Adequate GMP procedure for destruction of GMP documents is not in place.

Procedure for destruction for GMP documents is not in place; however it was a practice that in drop box only –

draft, obsolete copy and uncontrolled copy was placed for destruction.

CAPA Plan:

- ✓ As a corrective action SOP for destruction of documents has been implemented,
- ✓ A log book kept and activity done under QA.
- ✓ Training on SOP – for Destruction of documents; imparted

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THANK YOU

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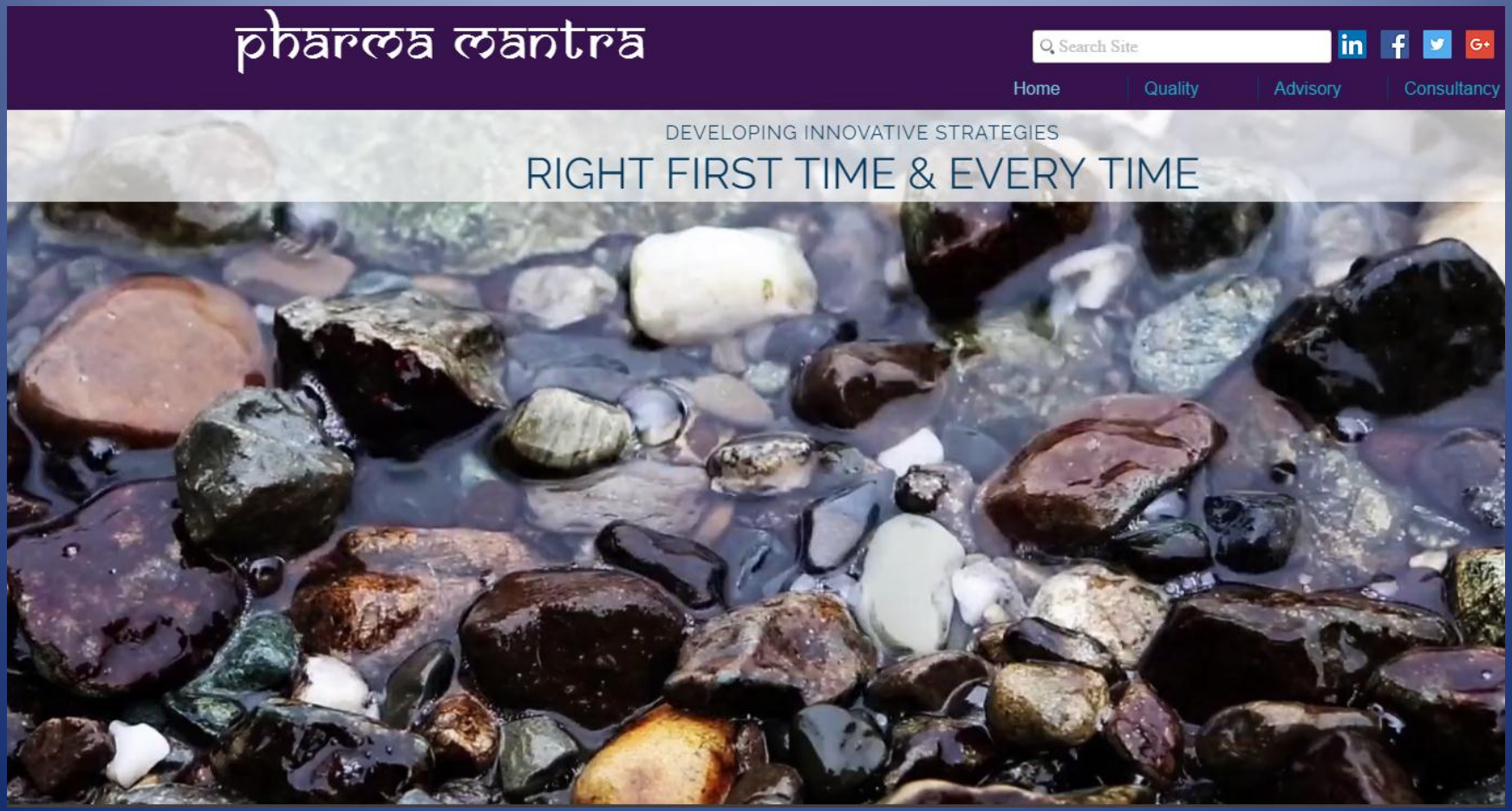

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- Quality & Compliance Strategy
- QMS Initiation, Implementation, Review
- Imbibe the Culture of Quality

More Info

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- Resource Management for SOC (state of control)
- Remediation Program
- GxP Compliance Strategies

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Udaykumar K. Rakibe

Founder

M.Pharmacy & MBA from Pune University – was mandated and given the task to execute and spearhead the proactive remediation in 2006 by Ranbaxy Lab. Ltd. In late 2011 he was recruited by Intas Pharma. to create a self-sustaining quality management system and enhance inspection readiness. Further, in 2013 he was hand-picked & recruited by Wockhardt Ltd., as Senior Vice President – Quality, to turn around the Quality Management, lead and manage the remediation of Quality initiatives.

Udaykumar is a quality professional with a dynamic career steering organizations through complex Quality & Regulatory challenges, transitions, building an empowered and talented workforce in the cross-cultural environment within highly competitive products and regulatory environment.

He began his career in Quality function in the Executive in-process QA with Glenmark Pharma Ltd. and then moved to different levels and organization spanning 26 plus years of hands-on and hardcore experience in the pharmaceutical regulatory environment. He has gained the domain experience in Quality by working 20 years' in Quality operations- out of twenty years last 11 years focusing and leading the Quality & Regulatory remediation. He has 7 years experience in Corporate Quality functions, overseeing the Developmental & filing of - Clinical, Analytical, Formulation, Devices. Has setup the Global Quality organization for the Contact Manufacturing in regulated and semi-regulated markets He has worked as a senior member of the Quality Team with Ranbaxy Labs Ltd., Dabur Pharma Ltd., Gland Pharma Ltd., IntasPharma Ltd., and Wockhardt Ltd.