CAPA ON CAPA

“We should work on our process, not the outcome of our processes”
Regulatory and Quality Solutions (R&Q) provides industry-leading regulatory and quality engineering services throughout the entire product lifecycle.
Paul Robinson, Senior Director of Regional Operations, R&Q

- 25+ years of domestic and international experience
- Previous: Covidien, Boston Scientific, BARD
- VP Quality - Maintained 20+ manufacturing plants worldwide
AGENDA

- Why?
  - Real world
    - Ready for an audit? What does the FDA look for?
  - CAPA regulations/requirements
    - 820.100

- CAPA system
  - Feeders
  - Data trending/evaluation/alerts
  - CAPA process
    - Risk management
  - System management

- The CAPA
  - Root cause analysis
  - Statistical tools
  - ELCD – Engineering, Logic, Common Sense, and Discipline!
WHY?
WHY?

- Real world
  - FDA audit
  - 80/20 rule – ever heard of that?
- Remember: CAPA is **not** an assignment or project. **It is a system.**
  - CAPA has been called the "immune system" of the Quality Management System. It must work for your organization to repair or improve itself properly.
Indications that your CAPA system may be feeling a little under the weather:

- CAPA metrics are inadequate for management understanding and control; too many, too few, too confusing
- CAPA projects are not progressing
- There is a very weak “CAPA culture”
- Your organization seems to have too many CAPA projects or they are languishing

We’ll discuss what to do in a few slides
WHY?

- Real world?
  - Managed correctly, it’s an opportunity for improvement
    - Reporting problems
    - Proactively addressing problems
    - Closed loop system

Don’t be afraid!
WHY ELSE?

- Regulations require it!
  - 21 Code of Federal Regulations (CFR) 820.100
    “Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action.”
  - ISO 13485:2003, 8.5.2, 8.5.3
    “The organization shall identify and implement any changes necessary to ensure and maintain the continued suitability and effectiveness of the quality management system through the use of the quality policy, quality objectives, audit results, analysis of data, corrective and preventive actions and management review.”

Even if not required, it is still smart to do. I should know, I’m an owl! We’re wicked smaht!
One more time. It is not an assignment or a project. It is a SYSTEM!
All feeders are equal, some more equal than others!
How?

- Tables
- Run charts
- SPC
- Pareto analysis
- Audits
- Complaints
- Etc.

- What’s important to monitor within your feeder system?
- How you are going to evaluate; and what are your alert/action limits?

<table>
<thead>
<tr>
<th>Feeder</th>
<th>Owner</th>
<th>Metric</th>
<th>Reporting Frequency</th>
<th>Method</th>
<th>Alert Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrap</td>
<td>Operations</td>
<td>% Scrap</td>
<td>Monthly</td>
<td>SPC</td>
<td>SPC Rules</td>
</tr>
<tr>
<td>Audits</td>
<td>Quality</td>
<td>% Schedule</td>
<td>Monthly</td>
<td>Limit</td>
<td>&gt;95%</td>
</tr>
</tbody>
</table>
CAPA PROCESS (RISK-BASED APPROACH)

Alert Triggered or Issue Identified

Initiate Corrective Action Request

1. No Action
2. Correction
3. CAPA
The CAPA Process

1. Problem Statement
2. Feeder/Source/Alert
3. Products Affected
4. Processes Affected
5. Departments/Functions Affected
6. Event Description/Summary
7. Initial Risk Assessment (with Rationale and Documentation)
8. Initial Frequency Assessment with rationale and documentation

Initiate Corrective Action Request

See risk-based decision matrix example next slide
## Procedure

### Risk Based Escalation

<table>
<thead>
<tr>
<th>Product and/or Business Risk</th>
<th>Frequency</th>
<th>Probability is so remote</th>
<th>Unlikely Probability</th>
<th>Occasional Probability</th>
<th>Moderate Probability</th>
<th>High Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negligible Patient Risk</td>
<td>1</td>
<td>NO ACTION REQUIRED</td>
<td>NO ACTION REQUIRED</td>
<td>CORRECTION</td>
<td>CORRECTION</td>
<td>CORRECTION</td>
</tr>
<tr>
<td>Business Performance Risk</td>
<td>2</td>
<td>NO ACTION REQUIRED</td>
<td>CORRECTION</td>
<td>CORRECTION</td>
<td></td>
<td>CAPA</td>
</tr>
<tr>
<td>Minor Patient Risk</td>
<td>3</td>
<td>CORRECTION</td>
<td>CORRECTION</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
</tr>
<tr>
<td>Internal Compliance Risk</td>
<td>4</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
</tr>
<tr>
<td>Moderate Patient Risk</td>
<td>5</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
</tr>
<tr>
<td>Documentation Compliance Risk</td>
<td>6</td>
<td>CAPA</td>
<td>CAPA</td>
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<td>CAPA</td>
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</tr>
<tr>
<td>Severe Patient Risk</td>
<td>7</td>
<td>CAPA</td>
<td>CAPA</td>
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<tr>
<td>Quality System Compliance Risk</td>
<td>8</td>
<td>CAPA</td>
<td>CAPA</td>
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<td>CAPA</td>
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</tr>
<tr>
<td>Catastrophic Patient Risk</td>
<td>9</td>
<td>CAPA</td>
<td>CAPA</td>
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</tr>
<tr>
<td>Regulatory Approval/Warning Risk</td>
<td>10</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
<td>CAPA</td>
</tr>
</tbody>
</table>
1. OK, but provide solid rationale...
**CAPA PROCESS**

1. Contain
2. Correct and dispose
3. Verify

Correction

Time to lean? Time to Clean!
CAPA PROCESS

1. Correction
   1. Contain
   2. Dispose
   3. Verify
2. Investigation
3. Solution verification/validation
4. Implementation
It would not be incorrect to assume that the CAPA system is one of, if not, \textit{THE} most important components of a Quality System, SO MONITOR its health and effectiveness and TAKE ACTION as needed!

- PAUL ROBINSON
1. Correction
   1. Contain
   2. Dispose
   3. Verify
2. Investigation
3. Solution verification/validation
4. Implementation

There is no Magic Wand!
E.L.C.S.D!

Ok, I’m done...
Avoiding...

Ready, FIRE, Aim!!!

OR

PROBLEM PARETO

I solved this one, I’m done!
ROOT CAUSE ANALYSIS & STATISTICAL TOOLS

- **Investigation**
  1. Problem description
     1. “What’s your problem?”
  2. Background information
     1. “How did I get here?”
  3. Source investigation
     1. “I know it’s in here somewhere.”
  4. Mining tools
     1. Dig, dig, dig

- **Implementation**
  1. Verification/validation!
  2. Verification/validation!
### Determining Probabilities

The probability of an event is the number of outcomes that the event occurs divided by the number of possible outcomes. For example, the probability of getting a “heads” on the flip of a coin is $\frac{1}{2}$ or .5 (heads/heads + tails). This tool can be used in determining complaint rates, defect levels, non-conformances, etc.
Measurement System Analysis

- Overall variation coming from a product or process is made up of the variation inherent in the product or process itself and an added component of variation coming from the measurement system.

- Measurement system variability can be broken down into two components, repeatability and reproducibility. Repeatability is the built-in variation of a measurement system and is calculated using repeated measurements made of the same variable under identical conditions. Reproducibility results when different conditions are imposed on measurements (different operators, set up methods, environment, etc.)

- The metrics often calculated are the Gauge R&R (repeatability and reproducibility) and the P/T ratio. The R&R represents the proportion of the overall variation coming from your measurement system. The P/T ratio is the amount of your specification taken up by measurement system variation alone.

- Before doing any analysis, it is crucial to have capable measurement systems. Values for R&R should be less than 30%. Values for P/T ratio should be less than 15%. Note-the required values can be changed based on risk.
Process analysis can be done by looking at various elements of data distribution.

**Shape**: Reviewing the shape of a distribution can help identify certain facts about a process. Is it skewed to one size or another? Do you have a bi-model distribution (potential of two sample populations?) Is it normal? Flat?

**Spread**: How variable is your process? Often defined by the standard deviation (square root of variance) or in some cases the range (difference of the high point versus the low point- sensitive to outliers)

**Central Tendency**: The center of the distribution.

**Temporal Element**: How does the process change over time? Typically run charts are effective ways to measure how a process changes over time.

**Capability**: Several terms are used to define capability.

- **Cp** is the short term/limited data capability of your product or process in meeting the range of your specification. It is the ratio of your short term variation divided by the width of your specification range. If barely capable, that ratio will be 1.0. If less than 1.0, your process is not capable. It does not take into account a distribution deviating from center specification.

- **Cpk** is the short/term limited data capability of your product or process. It does take into consideration any deviation from center. Cpk’s barely capable have a value of 1.0. If a process or product is less than 1.0, it is considered not capable.

- **Pp** is the long term process performance indicator. It is the ratio of your long term process variation divided by the width of your specification. It does not consider deviation from the center of the specification

- **Ppk** is the long term capability of your product or process. It does take into consideration any deviation from center. Ppks barely capable have a value of 1.0. If a process or product is less than 1.0, it is considered not capable.
**Relationships**

- **Scatter plots**
- **Box plots**
- **Pareto charts**
- **Pie charts**

**Scatter Plots** - The data is displayed as a collection of points on an XY chart. Each has the value of one variable determining the position on the horizontal axis and the value of the other variable determining the position on the vertical axis. The display enables an understanding of the relationship between the X and Y variable in addition to the strength of that signal.

**Box Plots** - is a standardized way of displaying the distribution of data based on the five number summary: minimum, first quartile, median, third quartile, and maximum. It is a convenient tool to display the spread and shape of a distribution.

**Pareto Charts** - a type of chart that contains both bars and a line graph, where individual values are represented in descending order by bars, and the cumulative total is represented by the line. This chart is very effective in identifying the top contributors to a condition. Remember the Pareto principle: “80 percent of the problems come from 20 percent of the sources”

**Pie Charts** - a convenient chart which clearly demonstrates the proportion of sources relative to a signal.
ROOT CAUSE ANALYSIS & STATISTICAL TOOLS

- Relationships
  - XY diagram - This is a very useful diagram demonstrating the relationship of an input (the X axis) to an output (the Y axis)
  - Correlation - is a measure of the degree of association between two quantitative variables. The value ranges from 1 (a very strong positive relationship), 0 (no relationship), to -1 (a very strong negative correlation). This is very useful in determining if changes with particular variable potentially influences, causes changes (or is the a correlation?) with another variable.
  - Regression allows you to quantify the relationship between one or many “input” variables against another “output” variable. The strength of that relationship is measured by a term known as R-squared. The value of R-square (described as a fraction or a percentage) is the estimate of the relationship that can be explained by the mathematical model/regression. For example if a regression is calculated and comes up with an R-squared value of .89 or 89%, then you would say that the 89% of the changes in output variable Y can be explained by the associated input variables in the model. Regression equations are very helpful in making “output” estimates using different values of potential “input” settings.
  - Hypothesis testing - is a powerful tool used in inferential statistics or decision making. It is used to project an inference with a certain probability, the relationship of two samples or populations. For example, a final statement would be “with 95% confidence, we can state that there appears to be no significant statistical difference between the two samples” Note: It does not say that they are the same, it just says that there is a relative confidence in saying we don’t see a signal.
  - ANOVA - is an analysis similar to a Hypothesis test however with an ANOVA, you are making an inference comparing multiple samples or population. Ultimately, you will be able to infer: “with 95% confidence, we cannot state that all of these samples is statistically equal to the others” (one or more is likely different)
QUESTIONS
THANK YOU!

For more information and to...

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