Implement a Risk-based approach to Change Control and Configuration Management

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Establish Risk Assessment Methodologies and Risk Levels
* What parameters are used to assess risk
* Who participates in the assessment
* How the resulting parameters are triaged
* Learn the importance of early identification of critical process parameters

Design the Change control and Configuration Management systems to leverage the Risk Assessment System
* Pre-define Change Control Levels based on identified risk with associated requirements
* Establish implementation work flow for Configuration Management based on the risk level
* Ensure buy-in prior to implementation by all parties (including Quality)
* Stream-line the change control and implementation timelines with efforts focused only on the areas required by the risk assessment

Interactive Exercise
* Using a real life example, participants will use risk assessment tools to determine the risks and mitigations, and then discuss the most appropriate implementation work flow.
Configuration management (CM) is a systems engineering process for establishing and maintaining consistency of a product's performance, functional and physical attributes with its requirements, design and operational information throughout its life.


For our discussion it is a Lifecycle Approach
Bases for approach

- 21 CFR 820 Quality System Regulations
- ISO 13485 Quality Systems
- GAMP
Applications

* Newly Developed or transferred products or processes – this entails a review of the entire process and associated equipment with the highest risk areas receiving the required focus.

* Changes to existing products, processes, equipment, or facilities – this entails a review of the changes, and their impact, with the highest risk aspects of the change receiving the required focus. Unchanged elements are documented with rationale as to why they will not require testing.
Risk assessment is used to identify the risks present and determine which will need to be addressed.

* Risk can be determined at the Product Level (i.e. tongue depressors vs. sterile injectables)
* Based on top-level product risk, the process can then be assessed for risk points
* Unit operations (or equipment) should be identified for impact as well
Several different types of risk analysis exist, for our discussion we will focus on pFMEA’s.

A pFMEA (Process Failure Mode Effect Analysis) is used to identify potential failures in a process (can be manufacturing, testing or even transactional) and objectively triage the risks so that the most significant can be mitigated.
pFMEA Steps

It includes the following major steps:

* Map the Process
* Identify failure modes
* Rank failure modes
* Identify Current Mitigations
* Identify Required Mitigations
A process is mapped with critical steps identified so that a risk analysis can be performed with a clear understanding of the steps.
Each step is assessed for potential failure modes (6M’s can be used as a basis to brainstorm these)

* Man
* Machine
* Method
* Measurement
* Materials
* Mother Nature (Environment)
Each Failure Mode is assessed for the following parameters

* Frequency of Occurrence
* Severity
* Level of Detection
For existing products or processes this should be based on historical trends, for new products or processes it can be based on similar existing ones, or technical knowledge. If unsure, assume above average occurrence.
Severity

* Reflects the harm or damage this failure mode will have, and can range from inconvenience or cosmetic defect, to product that doesn’t meet specifications or causes user or patient harm.
Accounts for the ability to identify the failure in process or prior to release or sale so that it can be addressed. Widgets with physical parameters or labels present opportunities for detection, while content uniformity or active ingredient strength would be more difficult.
What a template may look like

pFMEA Template.xlsx

* References:
Who Participates

* Process Subject Matter Expert (PSME) – May be Development, Technical Operations, or Manufacturing
* Quality
* Intended to be a group exercise to brainstorm various failure modes
* In practice a PSME may build to flowchart and present a starting point the group works off of.
Each failure mode is assessed for it’s Frequency, Severity, and LOD using a numeric scale.

For our discussion a scale of 1 to 5 is used
### Severity Ranking Scale

<table>
<thead>
<tr>
<th>Ranking</th>
<th>System Effect of Failure Mode</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Hazardous</td>
<td>Effect of failure mode potentially leads to harm to the patient/operator/service personnel/mfg personnel or potentially leads to damage of property/equipment/environment, in addition to any of the effects 2 through 4 below.</td>
</tr>
<tr>
<td>4</td>
<td>Major</td>
<td>Effect of failure mode is that product / item is inoperable; loss of primary function.</td>
</tr>
<tr>
<td>3</td>
<td>Moderate</td>
<td>Effect of failure mode is that product / item is usable, but some features not available; loss of secondary function.</td>
</tr>
<tr>
<td>2</td>
<td>Minor</td>
<td>Effect of failure mode is minor nuisance or annoyance.</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>There is no discernible effect.</td>
</tr>
<tr>
<td>Ranking</td>
<td>Occurrence</td>
<td>Qualitative Definition</td>
</tr>
<tr>
<td>---------</td>
<td>-------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ünstret to occur at a high rate. Failure is inevitable with new design, new application, or change in duty cycle/ operating conditions.</td>
</tr>
<tr>
<td>5</td>
<td>Highly Likely</td>
<td>The failure cause is expected to occur at a high rate. Failure is inevitable with new design, new application, or change in duty cycle/ operating conditions.</td>
</tr>
<tr>
<td>4</td>
<td>Frequent</td>
<td>The failure cause is expected to occur often. Failure is likely with new design, new application, or change in duty cycle/ operating conditions.</td>
</tr>
<tr>
<td>3</td>
<td>Occasional</td>
<td>The failure cause is expected to occur sometimes. Occasional failures are likely; history with similar designs and/or design simulations show occasional failures.</td>
</tr>
<tr>
<td>2</td>
<td>Remote</td>
<td>The failure cause is not expected to occur, but could occur a few times; Isolated failures associated with similar designs or in design simulation and testing.</td>
</tr>
<tr>
<td>1</td>
<td>Highly Unlikely</td>
<td>The failure cause is not expected to occur based on current knowledge. Very few failures are likely; no observed failures associated with almost identical design or in design simulation and testing.</td>
</tr>
</tbody>
</table>
# Detection Ranking Scale

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Detection</th>
<th>Criteria</th>
<th>Detection Type</th>
<th>Example Range of Detection Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Almost Impossible</td>
<td>Absolutely certain of non-detection</td>
<td>X</td>
<td>Cannot detect or is not checked</td>
</tr>
<tr>
<td>4</td>
<td>Remote</td>
<td>Controls have poor chance of detection.</td>
<td>X</td>
<td>Control is achieved with direct, indirect, or visual inspection.</td>
</tr>
<tr>
<td>3</td>
<td>Low</td>
<td>Controls may detect.</td>
<td>X</td>
<td>Control is achieved with double visual inspection or with charting methods such as SPC (Statistical Process Control) which result in delayed action. Control can detect only systemic errors.</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>Controls have a good chance to detect.</td>
<td>X</td>
<td>Control is achieved with error detection in station which cannot pass discrepant part or with charting methods such as SPC (Statistical Process Control) which result in immediate action. Control can detect both random and systemic errors.</td>
</tr>
<tr>
<td>1</td>
<td>Highly Likely</td>
<td>Controls certain to detect.</td>
<td>X</td>
<td>Discrepant parts cannot be made because item has been error-proofed by product or process design.</td>
</tr>
</tbody>
</table>
Identifying the CCP’s and Risks early

- Risk Analysis early in the process allow you to focus resources on the items with the most significant impact
- It also supports a risk based approach to later change control and validation
Pre-define Change Control Levels based on identified risk with associated requirements

- Change Control Levels can be pre-defined so that it isn’t rediscovered each time.
- Different methodologies can be applied to different changes (i.e. equipment changes or process changes)
Equipment changes can be classified into three overall categories –

* Identical Replacement – This requires it to be the same item from the same manufacturer with the same Part or Model Number.
* Fit, Form, Function – This requires it have the same critical physical dimensions and operating characteristics as the original.
* Change – Is not either of the above.
Requires documentation demonstrating that the item is identical as defined in your procedure

Best Practice would include a standardized form associated with the change control program that records the legacy and replacement items specifications and operating parameters to demonstrate they are identical.

Requires only Functional Verification using an abbreviated test form.
Requires documentation demonstrating that the item has the same fit (size, dimensions), form (same operations or methodology), and function (performance characteristics).

Again, best Practice would include a standardized form associated with the change control program that records the legacy and replacement items specifications and operating parameters to demonstrate they meet the requirements of FFF.

Requires Functional Verification using an abbreviated test form. May require performance testing based on criticality of the component to the process (i.e. terminal filtration vs pump motor).
True Change

* Is neither Identical or Fit Form Function.
* Typically a result of a planned change as opposed to emergency repair.
* Would require a lifecycle implementation approach with risk analysis of the change driving the validation and future change control requirements.
Establish implementation work flow for Configuration Management based on the risk level – Product Level

* The Implementation Work Flow should be based First on the Top Level Risk (Product).
* If the Product has a lower risk then the required Implementation Work Flow can be streamlined.
* A Higher Risk Product will require the supporting processes and equipment to be assessed.
High risk equipment will require a pre-established level of commissioning, qualification, change control, and maintenance.

Identified Lower risk (impact) items can have a reduced level of commissioning, reduced changes control requirements, and appropriate levels of maintenance.
Process Level

* Processes for higher risk products can be further assessed (earlier discussion) to identify the steps with the most impact so efforts for validation can be targeted.

* Can also be used to establish change control requirements going forward so that lower risk steps can proceed more quickly and cost-effectively.
Ensure buy-in prior to implementation by all parties (including Quality)

- Processes and Procedures for Risk Assessment and Implementation Management should be clearly described in procedures that are approved by quality.
- Procedures should identify the risk levels and appropriate controls so that the decision is made once, not each project.
- If agreement cannot be reached there should be a pre-determined escalation policy to keep projects moving in a timely, professional manner.
Stream-line the change control and implementation timelines with efforts focused only on the areas required by the risk assessment

* Within a project timeline, the areas identified as having greater risk require more stringent implementation and change controls
* If an area is not identified as high risk, it should not be held to the same standard