Applying ISPE Baseline Guide for Commissioning and Qualification (Second Edition) Within a CDMO

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Challenges CDMO's Face

Multiple product
Different phases of approval
Qualifying to accommodate all clients

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ISPE Baseline Guide for Commissioning and Qualification (Second Edition) Unknown Product/Process requirements (Chapter 29.5).

- **This is the first time that this is acknowledged as a challenge in a baseline guide**
- **What does this chapter say?**
- **How do we apply this process?**

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What Does the Chapter Say

29.5 Unknown Product/Process Requirements

For some types of projects, the product and/or process user requirements may not be known, whether completely or partially. This situation can occur for projects such as:

- Where product or process development work is ongoing
- Multi-product facilities, contract manufacturing facilities, or other situations where the product to be manufactured has not yet been identified
- Research and development facilities
- Clinical manufacturing facilities

There needs to be some basis for the design. For most projects, the user is able to define a generic set of process requirements and/or performance capabilities that the system should meet. These requirements become the basis for design and can serve as the process requirements. For some facilities, there may also be some general requirements that are derived from regulatory expectations, such as the expectation that aseptic filling will occur under ISO 5/Grade A conditions with unidirectional airflow.

System Risk Assessments and DRs can be performed. Individuals with expertise in the particular manufacturing process technology should be included in the team. The risk assessment should progress as normal, identifying CDEs that serve to control product quality risk.

Verification work is based on engineering specifications and carried out by SMEs. The verification work should include performance tests and determination of equipment operating capabilities (ranges, control accuracy, etc.) so that future product and process requirements can be readily evaluated against the capabilities of the process equipment and systems.

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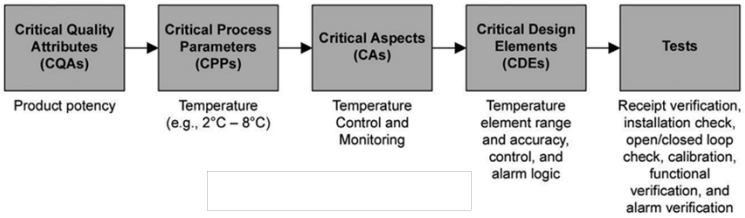
How do we apply this process

The next step in the process is System Risk Assessment (Chapter 4), the application of QRM in which a risk assessment of the direct impact system is used to examine the system product quality risk controls and to identify CDEs. It is important for the System Risk Assessment to be performed by Subject Matter Experts (SMEs) that understand the science of the process. CDEs are identified by examining the CPPs that need to be controlled to ensure product quality, as defined by the CQAs. CPPs are not only those that control delivery of drug substance or drug product CQAs, but can also be related to CDEs of packaged materials (e.g., ensuring inclusion of product inserts or variable data such as lot number and expiration date on labeling). The CAs of the process can be identified from the CPPs, and the CDEs of the system can be identified from the CAs. CDEs can also include features such as product contact materials of construction. Unacceptable risks are mitigated through the application of risk controls, which include the CDEs.

Figure 1.2 provides an example that illustrates the relationship between CQAs, CPPs, CAs, CDEs, and the associated testing.

Figure 1.2: Example of Automated Temperature Control and Monitoring of a Process Step



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Filler Qualification Test

What would you do to qualify a Filler to show Fit-For-Intended-Use?

- **Fill Accuracy (looking at all fill tubing types and bracketing the range)**
  - **Smallest Tubing** (e.g. 0.8 ± 0.03 % & 1.8 ± 0.03 %)
  - **Mid-Range Tubing** (e.g. 1.0 ± 0.03 % & 2.25 ± 0.1 %)
  - **Largest Tubing** (e.g. 1.5 ± 0.03 % & 3.0 ± 0.15 %)
- **Stoppering (Largest and smallest vials sizes)**
- **Crimping (Largest and smallest vial size)**
  - Base sample size off ANSI general Inspection Level II
  - e.g. lot size is 3000 therefore testing would process 1201 vials for stoppering and sample 125 against acceptance criteria.

Lot/Batch Size **1,201 to 3,200 vials** General Inspection Level II = Sample Size Code Letter K
Sample Size is 125 Units (Random Selection)

Lot Size[1]	Level II Normal AQL (Primary AQL Inspection)				Level II Single Tightened AQL (Secondary AQL Inspection)			
	Sample Size	Critical (Ac-Re)	Major (Ac-Re)	Minor (Ac-Re)	Sample Size	Critical (Ac-Re)	Major (Ac-Re)	Minor (Ac-Re)
2-8	2	0-1	0-1	0-1	2	0-1	0-1	0-1
9-15	3	0-1	0-1	0-1	3	0-1	0-1	0-1
16-25	5	0-1	0-1	0-1	5	0-1	0-1	0-1
26-50	8	0-1	0-1	1-2	8	0-1	0-1	1-2
51-90	13	0-1	0-1	1-2	13	0-1	0-1	1-2
91-150	20	0-1	0-1	2-3	20	0-1	0-1	1-2
151-280	32	0-1	0-1	3-4	32	0-1	0-1	2-3
281-500	50	0-1	1-2	5-6	50	0-1	1-2	3-4
501-1200	80	0-1	1-2	7-8	80	0-1	1-2	5-6
1201-3200	125	0-1	2-3	10-11	125	0-1	1-2	8-9
3201-10000	200	0-1	3-4	14-15	200	0-1	2-3	12-13

[1] Denotes all vials having passed 100% inspection

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Some Final Thoughts:

- **Most CDMO's know the platform process they are running even if they do not have a product to run.**
  - Such as a Fill Finish process.
  - They know what equipment is required to run the process.
    - **(Filler, Isolator, Rabs, ISO 5 room)**
  - Therefore they can qualify based on general product risk or patient risk and bracketing high and lows of equipment's capability.

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Questions?

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