10-6-2019

Workshop: Regulatory Gaps in Continuous Processing

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Regulatory Gaps in Continuous Processing Workshop ICB4 6th October 2019

Chair: Karen Sitney
Boehringer Ingelheim
Chair: Andrew Sinclair
Biopharm Services

Introduction to the session

Introduction to the questions (anything missing)
10 min

Working session groups

25 min

Report back 5 min/group

40 min

Wrap up
10 min

Timing

Logistics

Session

1.5 hours

~ 72 participants

7 groups

Each Group

Each table addresses one topic

Identifies other key points

One person per table to take notes

One person per table to present

Questions

Batch definition

Characterization & validation

Viral clearance

PAT

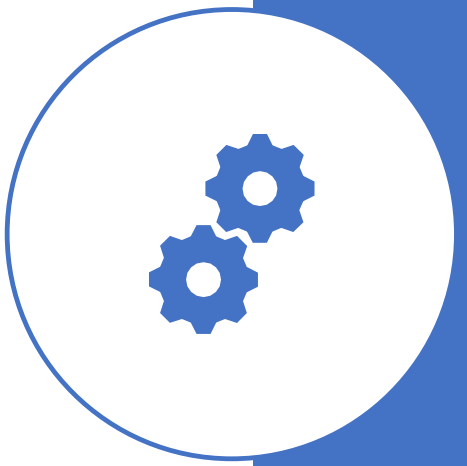
Bioburden

Sampling

Systems Integration

Group Topics

1. How do you define a batch for continuous & semi-continuous processes from a regulatory perspective?
2. Validation of continuous processes how do we meet current regulatory expectations?
3. How do we meet regulatory requirements requiring us to demonstrate viral reduction throughout the process?
4. What PAT technologies are needed to support robust in-line monitoring?
5. What are your in-process bioburden control strategies?
6. How and where are samples taken in a continuous process?
7. What are implications of system integration from a regulatory perspective?



Rank the Topics in Terms of Importance

How do you define a batch for continuous & semi-continuous processes from a regulatory perspective?

Validation of continuous processes how do we meet current regulatory expectations?

How do we meet regulatory requirements requiring us to demonstrate viral reduction throughout the process?

What PAT technologies are needed to support robust in-line monitoring?

What are your in-process bioburden control strategies?

How and where are samples taken in a continuous process?

What are implications of system integration from a regulatory perspective?

1. How do you define a batch for continuous & semi-continuous processes from a regulatory perspective?

- How did you/will you define a batch for continuous processes?
- What data did you use/would you use to justify the batch definition?
- What in-process pooling criteria did you/will you use for processes with variable PQ day to day?
- How much PQ variability is acceptable a particular release specification (e.g., glycosylation level, charge heterogeneity)? What data would you have to justify your stance?
- Are any of the above dependent on MOA (e.g., nuances in batch to batch consistency for a-fucose)?
- What are the implications of start up and shutdown

2. Validation of continuous processes how do we meet current regulatory expectations?

- Process characterization needs to account for the connectivity between steps. What is your approach for DOE – partition design vs testing isolated unit operations?
- How do you show the process is in a state of control?
- For instance, how do you demonstrate cycle-to-cycle consistency on downstream chromatography columns that are cycled 50-200 times?
- What data would you show to justify your stance?
- Are there different strategies for Upstream compared to Downstream

3. How do we meet regulatory requirements requiring us to demonstrate viral reduction throughout the process?

- How do you validate continuous virus inactivation?
- How do you validate VRF in a continuous process?
- How do you demonstrate viral clearance in a continuous chromatography column
- Do you use one membrane system continuously for 14-60 days?
  - Or do you change membranes every day?
  - What are the criteria to be used for changing them?

4. What PAT technologies are needed to support robust in-line monitoring?

- How do you show the process is in a state of control?
  - For normal steady state, start-up and shutdown considerations
- For instance, how do you demonstrate cycle-to-cycle consistency on downstream chromatography columns that are cycled 50-200 times?
  - What data would you show to justify your stance?
- Can we use PAT to adjust process perturbations in real time steering process to a optimum?
- How do you manage process deviations?

5. What are your in-process bioburden control strategies?

- What are your in-process bioburden control strategies for processes that operate continuously for 14 – 60 days downstream?
- Do you sanitize everything daily?
- Do you rely on sterile materials and filters and forgo sanitization?
- How do you change non active SU components (bags tubing)

6. How and where are samples taken in a continuous process?

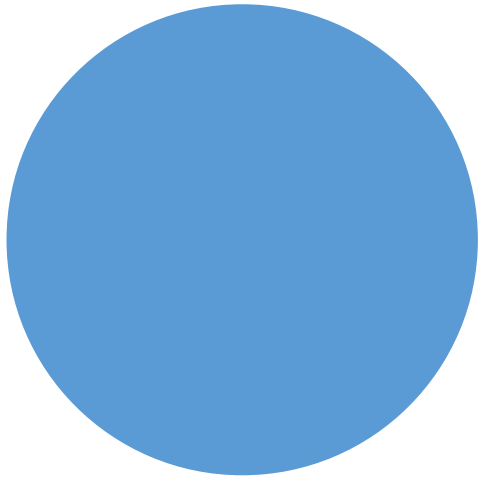
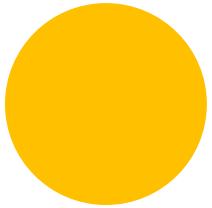
- Methods for taking a sample
- Frequency
- Device and controller delays
- Uniformity
- Start up vs. steady state

7. What are implications of system integration from a regulatory perspective?

- Do we need increased understanding of the interaction between linked unit operations?
  - To ensure stable operation
  - Resident time distributions
  - Implication for feedback/feedforward control
- Are there data management issues
- How do we deal with changes and disturbances?
  - Raw materials
  - Changes in process conditions (titre from the bioreactor)

Wrap Up 5 min/group

- What did you discuss
- Conclusions
- Unresolved issues
- Other points for consideration

Thank you