CONTROL STRATEGIES FOR INTEGRATED CONTINUOUS BIOPROCESSING

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Continuous Bioprocessing is perceived to deliver constant product quality and to achieve higher time space yields. This is not new. Other market segments run well established continuous processes successfully since decades. What do we need to do? Just establishing continuous single unit operations (e.g. SMB chromatography) will not suffice. We need to have an integrated look at the entire process chain and stringently use the following control strategies:

- Capture process variability of the preceding unit operation using advanced PAT tools. Just measuring CPPs will not suffice: We need RMAs and intermediate CQAs to be transparent across the process chain.
- Include above variability in the control strategy of the individual unit operations, carry out sound process characterization using data science tools.
- Have clear specifications for intermediate acceptance criteria (IACs), such as distributions of expected outputs of intermediate CQAs.
- Apply advanced process control strategies, such as multiple input multiple output controllers to robustly link process chain elements.
- Be aware that additional variability may occur along the life cycle. Hence, establish holistic manufacturing control strategies fulfilling Established Conditions (ECs) along ICH Q12 rationales.

This contribution aims at showing the central role of digital twins and data science in different control strategies: On the one hand, as we cannot measure all RMAs and CQAs of a process, we show how the process knowledge of single unit operations can be characterized by advanced data science tools and captured automatically in Digital Twins. We show how Digital Twins can be deployed for accelerating time to clinic as well as for continuous manufacturing. On the other hand, we can use integrated digital twins in production life cycle management for the identification of intermediate CQAs and can help when experiencing variabilities along Continued Process Verification (CPV) tasks.

![Image - Figure 1](Image)

*Figure 1 – Integrated Process Model analyzing the effect of CPP variability on the overall process and product quality*