N-MAB: A CASE STUDY SUPPORTING ADOPTION OF INTEGRATED CONTINUOUS BIOPROCESSES

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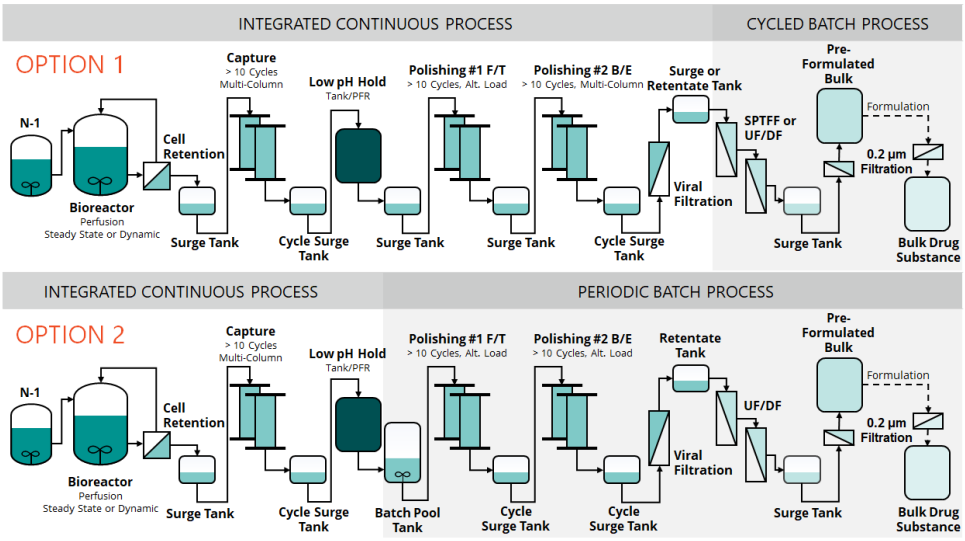
The A-mAb case study (2009) was created to stimulate discussion around how the core principles of QbD could be applied to the process development of a monoclonal antibody with examples of a multitude of real-world scenarios, as opposed to a singular approach. A-mAb was very successful in generating that discussion and impacted how process development was executed across the industry. Following a workshop on Process Intensification held at the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) in early 2020, it was decided to create a case study to support teaching and learning for both industry and regulators around adoption of advanced manufacturing process technologies such as integrated continuous bioprocesses for mAbs. This case study, named N-mAb, would provide examples of the implementation of different process options and associated process technologies that can drive an integrated control strategy, including considerations related to process development and characterization, process validation, and deviation management consistent with current guidance in place. Like its predecessor, A-mAb, the goal is to stimulate discussion and advance new concepts around integrated continuous bioprocesses. To make the discussion in this case study more manageable and still retain some diversity in process design, two major process options are discussed, based on the presence or absence of an intermediate batch surge tank as shown below, along with several minor options.



To illustrate different scenarios and the associated decisions involving variation in product quality, examples are developed based on an informed mock dataset which was generated from consensus industry experiences. N-mAb follows the evolution of an integrated control strategy from early clinical through process validation and commercial manufacturing as process understanding increases. It is important to note that the evolving versions of the control strategy are essential to assessing deviations and other aspects of managing the process in real time. A unique difference from A-mAb is that this N-mAb case study includes a discussion of the challenges involved in managing quality in real time as necessitated by a continuous process Since the control of adventitious agents often represents a unique subset of the overall control strategy and can be uniquely challenging for a continuous process, it is presented as a separate chapter. Another chapter expands on how decision processes can be constructed to manage deviations in either CPPs or CQAs. Examples of how the response to deviations can inform updates to a control strategy are given to demonstrate how continued learning cycles build upon the process knowledge established during Stage 1 Process Characterization. Overviews of these chapters as well as the threads linking the stages in the development of an integrated control strategy will be presented in the poster.