We are building a new disposable manufacturing system to support the development and manufacturing of mAb and mAb-related products. We have made choices that are different than many others in the field of continuous and integrated processing. These choices avoid many misperceptions about continuous processing, are consistent with a staged approach to implementation, and facilitate manufacturing in either large-scale disposable or stainless manufacturing facilities.

We have avoided the use of long-term steady-state perfusion. This mode of perfusion suffers from long development times, long manufacturing duration, extended Process Performance Qualification, large media consumption and perceived concerns about product quality variability and contamination.

The system uses a short duration (<15 days) non-steady state perfusion with perfusion rates as low as 0.3 bioreactor volumes per day. On-line UPLC is used to monitor product titer and quality. As a consequence of non-steady state perfusion operation, the integrated downstream is capable of handling day to day variability of 0.5g/L/day to 4g/L/day. The downstream avoids the use of SMB or PCC; rather, it integrates two batch chromatographic steps, a continuous virus inactivation step, and avoids in-process pooling. The product is stored after the second chromatography step for the duration of the batch. When the batch is complete, the pooled product is batched through a virus reduction filter and UFDF to make the bulk drug substance. Running these last two processes on the entire product pool at once allows an easy definition of a batch, without worry about pooling drug substance with different product quality profiles.

The result is an integrated, semi-continuous manufacturing process that mitigates many of the concerns felt by the batch-processing community.