

Rapid Process Development Enabled By Automated, Single Use High Throughput Technologies

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Efforts continue to speed the progress of new biologics from discovery through preclinical development to product launch. This is challenged by the move to novel modalities and managing the existing pipeline of products with limited resources. To provide rapid and right first time development, Merck Bioprocess Development applied automation and single use technologies from end to end, covering from cell line development to purified drug substance. For clone screening, laborious shake flask studies were replaced by a spin tube system with automated sampling and feeding capability. Further, inclusion of the Ambr15™ in the clone evaluation stage increased capacity and decreased process time both by 2X. Early stage upstream process development timelines were decreased 3-6X through the implementation of the Ambr15™ for medium and feed screening then to the Ambr250™ for process development. In addition, single use technology was implemented up to 2000L scale to accelerate the supply of drug candidates for development. Downstream processing development was moved from a platform that included small and preparative columns to mini column and micro tip formats operated on liquid handling arrays. This enabled execution of high resolution experiments to probe the design space, which resulted in more data with fewer resource investments in an equivalent time period. These technologies were supported by the development of high throughput analytical assays and tools. Titer and host cell protein assays were moved from an ELISA/HPLC platform to a rapid microfluidic Gyrolab™ platform. This change alone reduced assay time 3X while increasing throughput 10X. Taken together, the investment in automated high throughput technologies well positioned Merck Bioprocess development to execute on its mission of delivering robust and well characterized processes with accelerated timelines.