DEVELOPMENT AND APPLICATION OF AN ADVANCED PAT STRATEGY TO AN INTEGRATED CONTINUOUS DRUG SUBSTANCE MANUFACTURING PROCESS

Chao-Hsiang “Richard” Wu
chaow@amgen.com
Neil Soice, Nitin Rathore, Gang Xue, Becky Chan, Jette Wypych, Rohini Deshpande, Chetan Goudar, Amgen Inc.

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Integrated continuous biomanufacturing and associated process intensification offer multiple strategic, business, and financial advantages to a manufacturing network. Substantial progress continues to be made in the advancement of both upstream and purification unit operations and their integration. However, to develop optimal continuous processes and to fully realize the benefits of integrated continuous biomanufacturing, there is a need for the development and deployment of robust PAT paradigms. In addition to enabling real-time monitoring and control of process and product quality attributes, a well-executed PAT framework can help design a robust integrated control strategy and also enable real time product release.

We present the development of an advanced PAT framework to support both upstream and downstream components of an integrated continuous biomanufacturing process.

- On-line, real-time product quality attribute assays such as mass spectrometry-based multi attribute method (MAM), glycosylation profile, aggregation, charge variant, titer, metabolite, etc. were connected to the DS manufacturing process (Figure 1) by the Amgen proprietary sampling and sample preparation technologies.
- At-line walkup assays for endotoxin, pH, cell viability, product concentration, step yield, osmolality, identity, appearance, color, clarity, sterility, subvisible particles, etc. as the on-the-floor compendial assays.
- In-line sensor probes for viable cell density, nutrients, and product titer.
- Implemented more than 50% of all in-process and release assays on-the floor. Few hundreds of testings were executed online and autonomously throughout the course of DS manufacturing and achieved an overall ~77% time reduction from months to days for material disposition.

Robust and attribute-focused PAT deployment enables advanced PAT strategy. The integration of process-agnostic attribute testing framework to the manufacturing process through the state-of-art automation allows real-time attribute-based monitoring and control strategy to ensure product quality, process efficiency, and expedited material disposition.

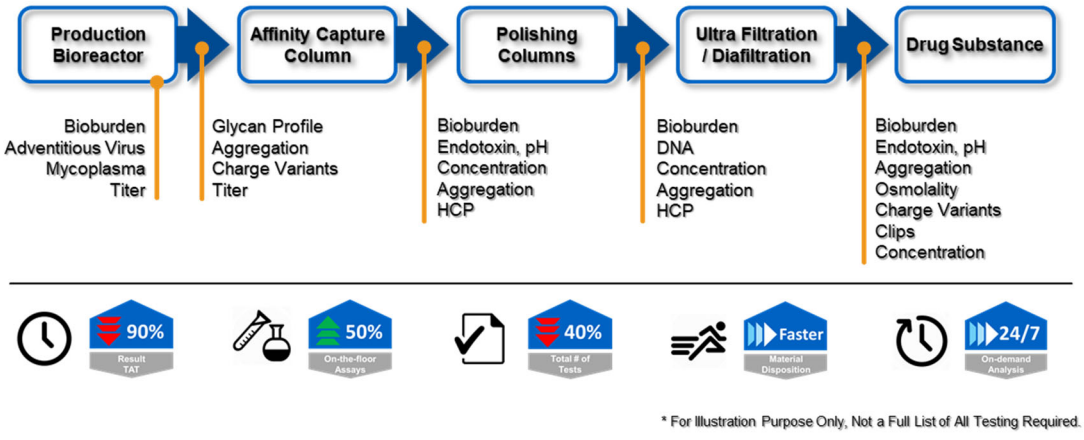

Figure 1 – Deployment of Advanced PAT Framework to the Integrated Continuous Drug Substance Manufacturing Process