BRINGING FLEXIBILITY TO INTEGRATED CONTINUOUS BIOMANUFACTURING

Loïc Fejoz, Merck, USA
loic.fejoz@merckgroup.com
René Reinbigler, Merck, USA
Eugene Tung, MSD, USA
Christopher Rode, Janssen R&D, LLC , USA
Paul Randolph, Janssen R&D, LLC, USA
Brian Polilli, Janssen R&D, LLC, USA
Roger Hart, NIIMBL, USA

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Flexible technologies, equipment, and facilities address several challenges facing the biopharmaceutical industry. First, demand for pharmaceuticals is difficult to forecast and can vary dramatically over the product lifecycle. As a result, the optimum production scale is often different than that for which it was originally developed. Second, it is not currently feasible to easily consolidate products operating at different scales within the same facility. Finally, personalized and targeted medicines are transforming the product mix toward small volume products, each requiring separate technology transfer and likely differing production lines. Consequently, to maximize facility and asset utilization, agile and flexible solutions are required to minimize product changeover time and ultimately drive down manufacturing costs.

To address these challenges, NIIMBL[1] has developed an ambitious 10-year collaborative program to transform the biopharmaceutical manufacturing industry. Key to achieving this vision is designing, developing, and demonstrating plug-&-play solutions that offer component interchangeability, system reconfigurability, system verification for fit-for-purpose, system portability, and adjustable-rate production. This presentation will focus on our component interchangeability achievements, the first step along this strategic flexibility roadmap that provides the technological foundation for ultimately achieving the vision.

In this presentation, we demonstrate interchangeability of system components during the execution of a unit operation without the need for pre-configuration or any electrical rewiring nor software code updates. Through this demonstration the system maintains data continuity. This example involves the use of like-for-like dissolved-oxygen (DO) probes from different vendors to control the DO concentration within a 50L single-use bioreactor (SUB) and can be generalized to other like-for-like use cases beyond DO. Leveraging existing and anticipated standards (e.g., NAMUR, BioPhorum Operations Group, OPC Foundation) necessary for future-ready and technology agnostic solutions, we have demonstrated the DO control of a SUB can be changed to an external smart DO probe through:

- Connecting the alternative smart DO probe to the SUB through an available network
- The SUB automatically recognizing the new hardware, establishing the communication network, and determining fit-for-purpose of the new probe
- The ability to select the new probe for recipe-controlled DO without the potential need for system requalification

The capabilities described above enable true plug-&-play, with automated component interchangeability occurring within minutes. We will conclude the presentation by providing a preview of the next steps on the roadmap to delivering the 10-year flexibility vision.

[1] Erickson, J, Baker, J, Barrett, S, et al. (2021). End-to-end collaboration to transform biopharmaceutical development and manufacturing. *Biotechnology Bioengineering*. 118, 3302– 3312. https://doi.org/10.1002/bit.27688