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Innovating for Speed, Complexity and Sustainability in Pharmaceutical Development and Manufacturing

In the late 2000s, the Food and Drug Administration championed the concepts of advanced manufacturing for the pharmaceutical industry starting with the basic elements of quality by design like capturing robustness in design spaces, mostly enabled by design of experiments and process analytical technology (ICH Q8/9/10; FDA Guidance for Industry "PAT — A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance" 2004). The initial mention of mathematical tools and process controls gave way to what is now advanced analytics and monitoring systems and created the path for access to data that enables multivariate models and continuous processing. Since then, modeling techniques, solutions and computational capabilities have continued to evolve in all aspects of pharmaceutical development and the successful, yet limited, adoption of continuous processing has captured most of the innovation in the pharmaceutical industry, whether chemical, drug product or biological processes. Given the agreement among industry, government, and academia on the benefits to quality, flexibility, and footprint for continuous processing (ICH Q13; Lee *et al*.) these efforts have been the culmination of the innovation in process understanding and controls. Therefore, in the last 20 years pharmaceutical process innovation has focused on driving quality into the process and modernizing aspects of process control, monitoring, and delivery of critical attributes.

So after 20 years into the journey of innovation and the advanced manufacturing agenda, where are we headed? The National Academies of Science, Engineering and Manufacturing hosted a collaboration between FDA, industry and academia to define the next generation advanced manufacturing (Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations (2021)). The output report concludes that the innovations we are most likely to see in the next decade are new routes to produce drug substances, process intensification, additive manufacturing, advanced process control and automation, and modular systems, even if these represent the most challenging to current regulatory frameworks. Today, the biggest challenges facing the pharmaceutical industry today speed of development due to a fundamental increase in breakthrough discoveries, lack of manufacturing capacity, sustainability, and overall complexity of molecule profiles. The innovation to face these new challenges will require true retooling of regulatory and industry standards to allow modeling enabled process development, higher utilization of data into knowledge, and doing 'more with less'. The talk will discuss aspects of this innovation agenda and explore how we can define future success.

Lee, S.L., O'Connor, T.F., Yang, X. *et al.* Modernizing Pharmaceutical Manufacturing: from Batch to Continuous Production. *J Pharm Innov* **10**, 191–199 (2015). https://doi.org/10.1007/s12247-015-9215-8