PHARMACEUTICAL ONLINE

Guest Column | February 22, 2021

FDA Steps Up Support For Advanced Manufacturing Technologies

By Bikash Chatterjee, CEO, Pharmatech Associates

The latest article by FDA Commissioner Hahn[1] is one of a string of communications and guidances emphasizing the agency's support for the adoption of advanced manufacturing technologies (AMTs) and processes. The FDA has defined advanced manufacturing as new and emerging approaches for the production of medical technologies that can improve drug quality, address shortages of medicines, and speed time-to-market. The agency recognizes that AMT subsumes a broad swath of production techniques, including:

- The integration of novel technology approaches;
- The use of established techniques in a new or innovative way;
- Applying production methods in a new domain where there are no defined best practices or experiences.

This move is part of a broader realization that the FDA must proactively evolve and prepare itself to accommodate the rapidly changing initiatives within industry that include the adoption of digital technologies and Industry 4.0, in addition to AMTs. The renewed emphasis on AMTs has been driven in part by a desire to strengthen our national public infrastructure and partly in response to weaknesses revealed in our national supply chain for essential medicines and devices because of recent hurricanes and the global shutdown from COVID-19.

Support For Advanced Manufacturing

The FDA's commitment to innovation goes beyond providing guidance alone. In 2019[2] the agency signed a Collaborative Research and Development Agreement (CRADA) with the University of Delaware on behalf of the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). This CRADA will enable the FDA and NIIMBL to support investments in regulatory science research and training needed to foster advanced manufacturing innovations in areas such as continuous manufacturing, on-demand manufacturing, and advanced process control technologies.

In its latest move to encourage the broader adoption of AMTs, the FDA has entered into a memorandum of understanding (MOU) with the National Institute of Standards and Technology (NIST) that combines the strength of FDA's regulatory expertise and NIST's globally recognized precision characterization and standards. The MOU is significant because it takes the next step in providing guidance and resources to an industry that has been hesitant to pursue AMTs because of the compliance and regulatory uncertainties. It brings NIST's world-class measurement and testing facilities, along with its relationships with key industry organizations through its Advanced Manufacturing National Program Office, to the FDA's efforts to promote the adoption of AMTs. It also provides direct points of contact between senior leadership and collaborative links to subject matter experts to accelerate development and implementation of best practices for AMTs.

The COVID-19 Catalyst

If there is a silver lining to the COVID-19 pandemic, it is the urgency with which the pharmaceutical and medical device industries pushed new technologies and principles to the forefront. This MOU has the potential to be a catalyst for a pharmaceutical and biotech industry that has been historically slow to adopt new technologies. Part of that reluctance could be attributed to the absence of clear guidance by the FDA or EMA or the lack of clear industry best practice standards relating to the characterization and control of these AMT processes as they relate to established CMC and quality considerations. It can be argued that until COVID-19, there was limited impetus to invest and take on the risk of AMTs. To that end, the FDA has been busy providing guidance for everything from continuous manufacturing to its most recent white paper on the application of artificial intelligence and machine language.[3]

CDER, CDRH, CBER AMT Support And Advocacy

The FDA's MOU with NIST is one of several agency initiatives designed to drive adoption of AMTs. The Center for Drug Evaluation and Research's (CDER) Emerging Technology Program[4] already in place is designed to address drug sponsors' biggest anxiety with AMT adoption: the potential time lost as FDA reviewers familiarize themselves with the new technology applications. Through the program, industry representatives can meet with Emerging Technology Team (ETT) members to discuss, identify, and resolve potential technical and regulatory issues regarding the development and implementation of a novel technology, prior to filing a regulatory submission. The Center for Biologics Evaluation and Research **(**CBER) has also established the CBER Advanced Technologies Team (CATT) as part of its

Advanced Technologies Program,[5] which mirrors CDER's ETT to promote dialogue, education, and input among CBER staff and between CBER and prospective innovators/developers of advanced manufacturing technologies that are intended to be implemented in CBER-regulated products.

CDER and CBER have partnered to create a Center of Excellence for Advanced Manufacturing, with the goal of enabling science- and risk-based assessments and inspections of drug and biological product manufacturers, establishing best inspection practices, and providing training to staff related to novel manufacturing technologies.

As a result of the pandemic, CBER is focusing a great deal of energy on the adoption of advanced manufacturing methods for critical vaccines, with the intent of demonstrating the advantage AMTs could provide in rapidly ramping up the vaccine supply or by efficiently modifying certain vaccines to address regional variants and emerging infectious diseases.

The push to promote innovation is not limited to drug therapies. The Center for Devices and Radiological Health's (CDRH) Case for Quality Program[6] has been in place since 2011 and is intended to help the FDA identify device manufacturers that consistently produce high-quality devices. It will allow the FDA to identify successful manufacturing practices to help other device manufacturers raise their manufacturing quality levels. CDRH is building upon this program by establishing what it calls an AMT clearinghouse for advanced technologies such as high-performance computing, digitalization of production, modeling, and advanced robotics. The plan is to provide non-proprietary information regarding successful implementation techniques and strategies and promote the adoption of more effective and efficient means of manufacturing.

Reshoring And Continuous Processing Become Strategic

There is no doubt the global interest in reshoring has sparked renewed interest in evaluating AMTs for critical components of the essential medicines and products global supply chain that have been outsourced to other countries. The economic considerations that drove these manufacturers and suppliers outside must be addressed unless the government is to forever subsidize these industries.

While most of the U.S. pharmaceutical industry applies a batch processing approach rather than a continuous manufacturing approach, the advantages of continuous process over batch processing are significant. Batch manufacturing involving multiple discrete steps is based upon sampling and offline testing and typically requires longer cycle times for processing. Continuous processing, by contrast, means that drug components are processed continuously between unit operations, eliminating hold times between work centers, reducing the likelihood for human error, and carrying the potential to respond more rapidly to market changes. This could be a big advantage when looking at certain essential medicines and at therapies on the drug shortages list. So why hasn't the industry jumped on the continuous manufacturing bandwagon? The reality is the transition to continuous manufacturing is capital intensive and requires more advanced process characterization capability. Developing a control strategy for a continuous process is a multi-modal proposition that requires sophisticated statistical and analysis tools that many drug sponsors and CDMOs do not routinely retain in-house.

To that end, the MOU with NIST could have a significant effect by providing technical guidance to the industry in terms of the tools and techniques to employ for characterizing and developing a process for active pharmaceutical ingredients (API) and drug products.

Conclusion

Historically, one of the biggest concerns drug sponsor innovators have voiced in pursuing and adopting AMTs has been the potential time lost in time-to-market because of the FDA's unfamiliarity with new and emerging technologies. However, the FDA has taken significant steps to not only familiarize itself with new and emerging technologies but also provide timely guidance on the compliance and regulatory expectations for these new technologies. The latest MOU between FDA and NIST has the potential to provide yet another critical technical guidance that could greatly standardize the approaches to implementing AMTs, such as those used in continuous manufacturing. The economic considerations that have impeded such an approach remain, but national initiatives such as reshoring provide the opportunity to more broadly implement and refine these technologies and evaluate whether the promises of these technologies can be realized, in practical terms.

About The Author

Bikash Chatterjee is CEO of Pharmatech Associates. He has over 30 years' experience in the design and development of pharmaceutical, biotech, medical device, and IVD products. His work has guided the successful approval and commercialization of over a dozen new products in the U.S. and Europe. Chatterjee is a member of the USP National Advisory Board and is the past chairman of the Golden Gate Chapter of the American Society of Quality. He is the author of Applying Lean Six Sigma in the Pharmaceutical Industry and is a keynote speaker at international conferences. Chatterjee holds a B.A. in biochemistry and a B.S. in chemical engineering from the University of California at San Diego.

References

1. Accelerating the Adoption of Advanced Manufacturing Technologies to Strengthen Our Public Health Infrastructure, https://www.fda.gov/news-events/fda-voices/accelerating-adoption-advanced-manufacturing-technologies-strengthen-our-public-health

2. https://www.prnewswire.com/news-releases/niimbl-and-fda-sign-new-agreement-to-support-advanced-innovation-in-biopharmaceutical-manufacturing-300894194.html

3. https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device

4. https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/emerging-technology-program

5. https://www.fda.gov/vaccines-blood-biologics/industry-biologics/cber-advanced-technologies-program

6. https://www.fda.gov/medical-devices/quality-and-compliance-medical-devices/case-quality

Comments

Login

There are no comments posted yet. Be the first one!

Post a new comment

Enter text right here!

Comment as a Guest, or login:

Name

Displayed next to your comments.

Email

Not displayed publicly.

Website (optional)

If you have a website, link to it here.

Subscribe to None

Submit Comment