



Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues and Recommendations

Board on Chemical Sciences and Technology
Committee to Identify Innovative Technologies to Advance
Pharmaceutical Manufacturing

Charge

- Identify emerging technologies with potential to advance pharmaceutical quality and modernize manufacturing for CDER-regulated products
- Describe technical and regulatory issues associated with innovations
- Recommend how to overcome regulatory issues to facilitate adoption of novel technologies

Key Manufacturing Innovations on the Horizon

- New routes to synthesize drug substances.
- Co-processed active pharmaceutical ingredients.
- Process intensification to create more efficient, higher-yielding processes and enable smaller manufacturing footprints.



Key Manufacturing Innovations on the Horizon

- Additive manufacturing technologies that can tailor and customize characteristics of a drug product.
- Advanced process control, automation, AI/ML to support real-time operation and management of manufacturing (Industry 4.0,).
- Modular systems towards creating integrated, flexible, and distributed manufacturing networks.



Challenges Imposed by Regulatory Process

- Product & Technology review process
- Alignment of Incentives for Manufacturing Innovation
- Global Harmonization
- Post-approval Change
- FDA internal limitations



Committee Recommendations

Advance innovative mechanisms for evaluating technology outside product approvals. CDER should create new mechanisms and evaluate, expand, and consolidate existing pilot programs that allow consideration of innovative technology outside individual product submissions.



Committee Recommendations

Expand the scope and capacity of the Emerging Technology Program and the Emerging Technology Team. Recommended actions: (1) dedicate independent funding to the ETT, (2) expand the dedicated ETT staff, (3) broaden the criteria for entry into the program, and (4) increase transparency of the capacity of the ETT and program outcomes.



Committee Recommendations

Expand the leadership role in global regulatory harmonization efforts. CDER should increase dedicated resources and incentives to support greater emphasis on consistency in implementation of existing ICH guidelines and to enable leadership in ICH working groups to accelerate harmonization.



Committee Recommendations

Strengthen expertise in innovative technology throughout CDER. CDER should increase technical fluency among its scientists through such actions as priorities in hiring and retention practices and ensuring that staff-development plans support continuous education on innovative technologies.



Committee Recommendations

Increase external engagement to facilitate innovation and increase awareness of readiness of CDER to evaluate innovative technology. Recommended efforts: increase engagement, increase visible leadership, and leverage agency investments, extramural-research funding mechanisms, and partnerships.



Innovations in Pharmaceutical Manufacturing on the Horizon: A Virtual Dissemination Workshop

October 28-29, 2021

Community Response

- *Technology Innovations confirmed; post-Covid reprioritization*
- *Importance of Regulatory actions but also industry practices*
- *Importance of Creating Innovation Incentives re-emphasized*

FDA OPQ Response

- *Emerging Technology Program 2.0: expanded model*
- *Framework for Regulatory Advanced Manufacturing Evaluation*
- *Advanced Manufacturing Science & Research: internal & external*



Concluding Statement

- *There is strong consensus that advanced manufacturing technologies can and must play central role in creating a future agile, flexible industry that can produce high-quality drugs reliably.*
- *Incentives for adoption of innovations is key issue going forward, esp for existing products*

