FDA Initiatives to Support Implementation of Pharmaceutical Manufacturing Innovations

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INNOVATIONS IN PHARMACEUTICAL MANUFACTURING ON THE HORIZON: A VIRTUAL DISSEMINATION WORKSHOP – October 29, 2021

The Current Landscape

- **Context:** Advanced manufacturing technologies are emerging rapidly.
- **Vision:** "A maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs."
- **Approach:** Review the current regulatory landscape and ensure readiness for new technologies: *manufacturing innovation in the next 5-10 years*.

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Framework for Regulatory Advanced Manufacturing Evaluation (**FRAME**)

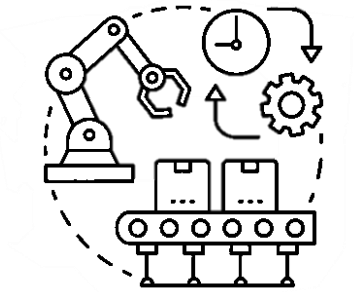
Getting Started

- Funded the National Academies to **gather public input** on emerging technologies.
- Described **Industry 4.0** and the future of pharmaceutical manufacturing

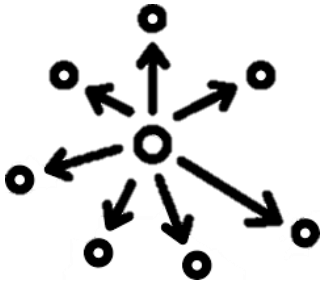
*Arden, N. Sarah, et al. "Industry 4.0 for Pharmaceutical Manufacturing: Preparing for the Smart Factories of the Future." *Int J Pharm* (2021): 120554.

Narrowing the Scope

End to End Continuous Manufacturing (E2E CM)



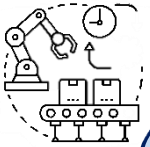
Distributed Manufacturing (DM)



Point of Care (POC) Manufacturing

Artificial Intelligence (AI)

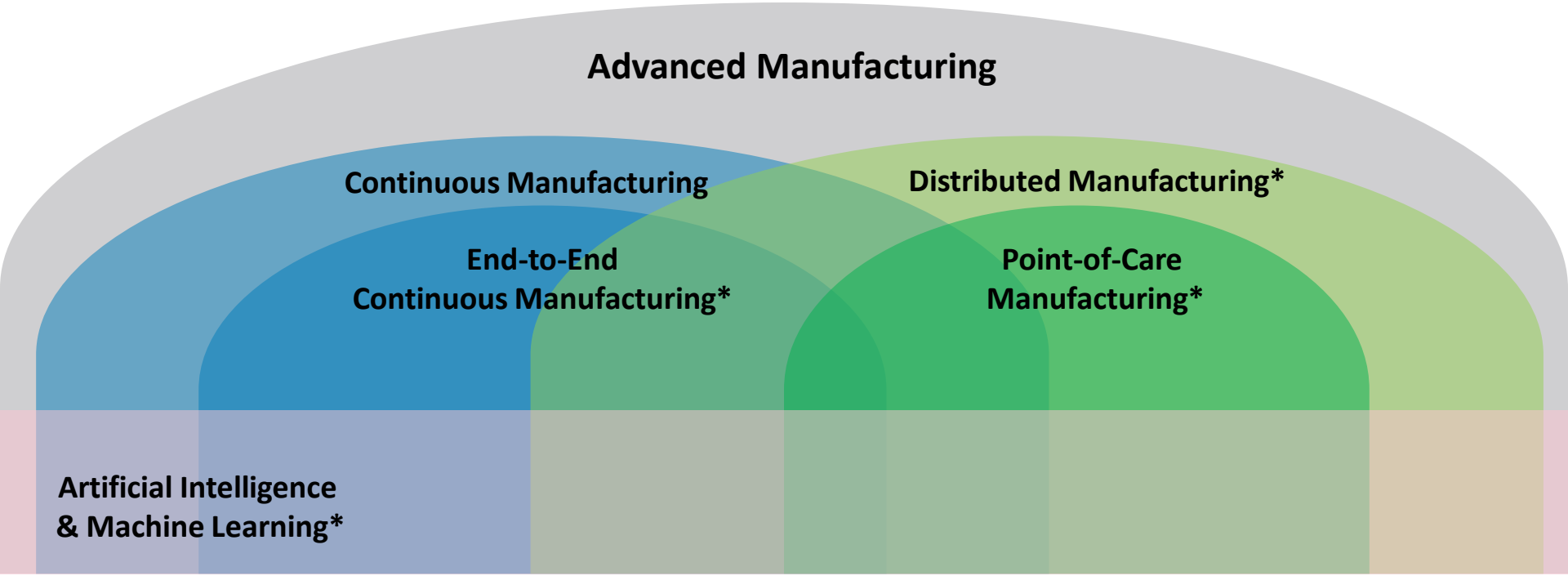
AM Technologies



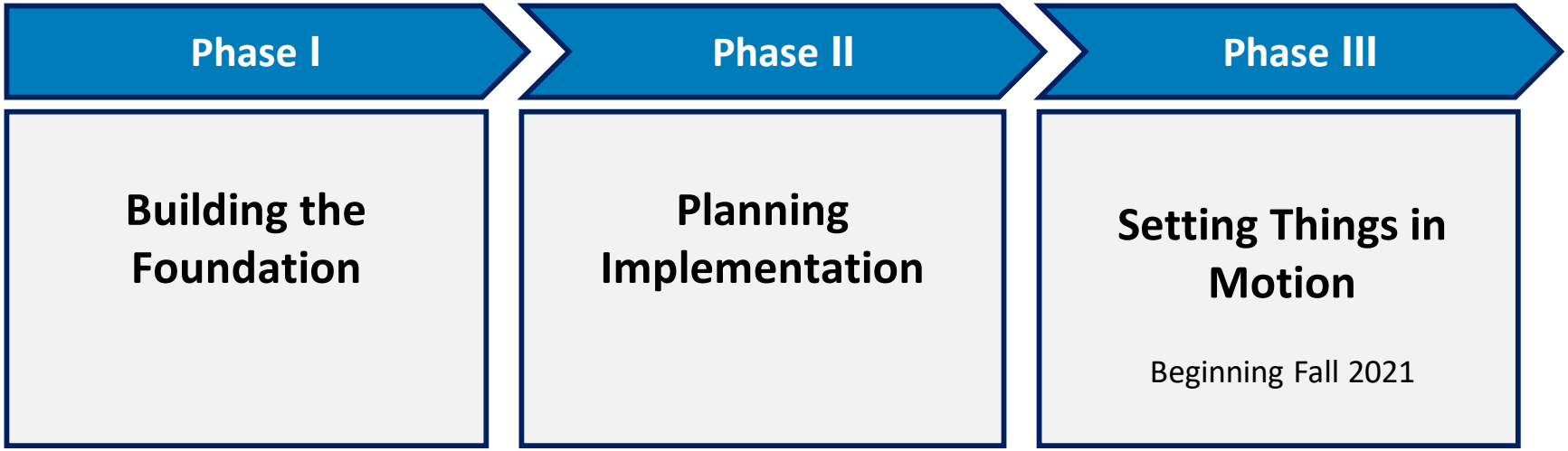
End-to-End Continuous Manufacturing (E2E CM)

A ***fully integrated process*** in which raw materials or chemical intermediates are continuously fed into and transformed within the system and finished drug products are continuously removed from the system.

Ecosystem of AM Technologies



Phased Approach to FRAME

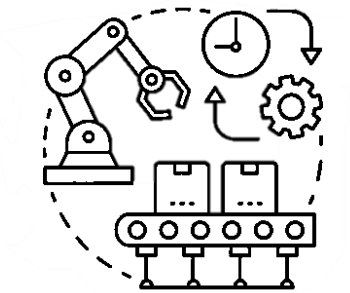


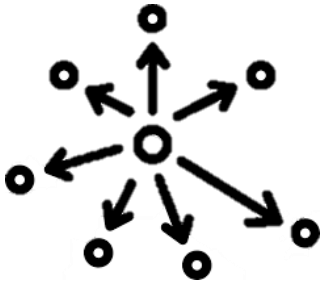
Phase I: Building the Foundation

- Assessed existing guidance, regulations, and statutory authorities for **gaps and pain points**.

Examples of Gaps and Pain Points

- Applicability of **regulatory terminology or guidance**
- Holes in **drug application requirements**
- Ability to comply with current **regulations and standards**



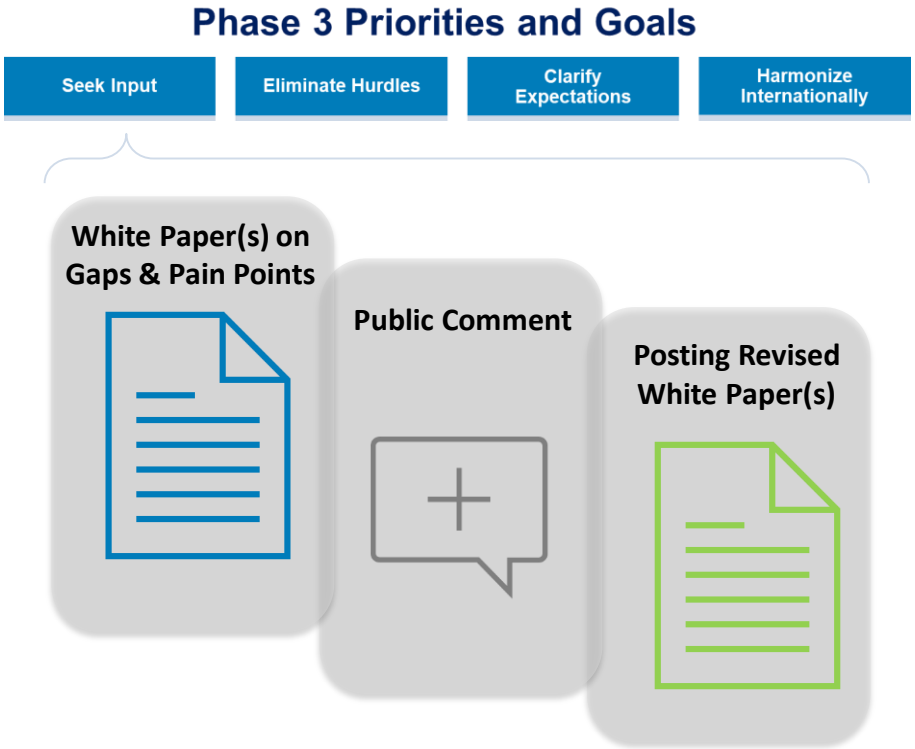


Phase II: Planning Implementation

- Conducted in-depth impact analyses to make **recommendations for the regulatory framework**.

Phase III: Setting Things in Motion (Fall 2021)

- Increasing **public outreach.**
- Soliciting **public input** to further inform our thinking.
- Beginning **implementation** of components of a regulatory framework.

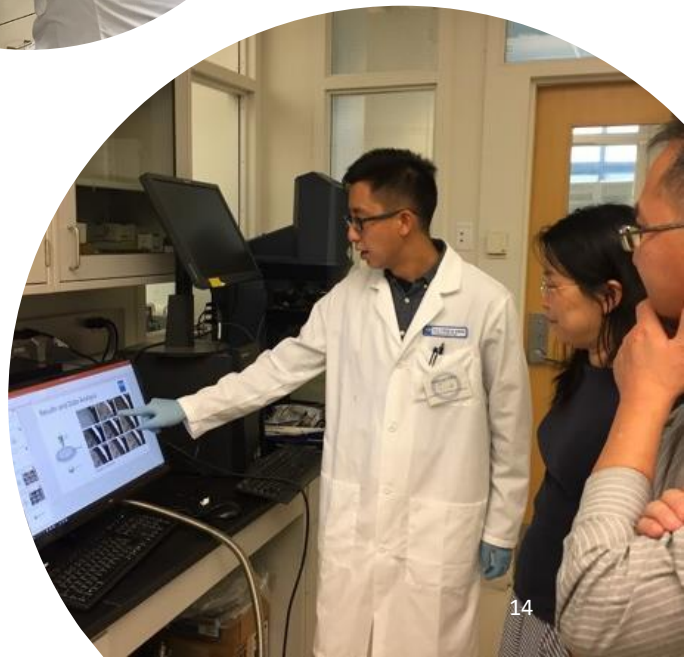


Framework for Regulatory Advanced Manufacturing Evaluation (**FRAME**)

- Establishing an appropriate regulatory framework to **keep pace with innovation** is crucial for public health.
- Pursuing **a systematic approach** for a regulatory framework requires continued scientific and policy expertise.
- Continuing to **seek public input** is a key component of the implementation of a cohesive regulatory framework.

OPQ Science and Research

- **Enhance** the FDA's capacity for evaluating and monitoring drug quality, safety, and efficacy
- **Modernize** current regulatory pathways or **indicate** a new regulatory pathway where there is currently none
- **Address** regulatory and scientific issues that are mission critical
- **Maintain** a state of *science and research readiness* that anticipates potential regulatory needs while allowing for rapid response to emergent regulatory issues



OPQ Product Development Science Capabilities

Intramural Research
Novel Manufacturing Methods (10 projects)
Precision Analytics (16 projects)
Advanced Manufacturing of Biopharmaceuticals (11 projects)
Manufacturing of Glycoproteins (3 projects)
Manufacturing of Synthetic Nucleic Acid Sequences (1 project)
Process Modeling, and Artificial Intelligence (AI)/ Machine Learning (ML) (4 projects)

Projects generated more than 65 internal reports and publications

Continuous perfusion bioreactor

3D Printing

High resolution mass spectrometry

Product Development Science Program - Extramural

Extramural collaborations via grants and contracts
Industry 4.0 and Smart Manufacturing (3 projects)
Novel Manufacturing Methods (6 projects)
Novel Process Analytical Technologies (4 projects)
Process Modeling and Simulation (2 projects)
Advanced Manufacturing Training (1 project)

Projects generated more than 13 publications

Continuous manufacturing of lipid nanoparticles (UConn)

End to End continuous manufacturing (Continuus)

Continuous bio-purification (Chromatan)

Continuous direct compression (Ruggers)

Summary of Outcomes and Impact

- Directly supported ETT feedback and application assessment for over 10 ETT projects
- Policy and guidance development
  - Informed development of ICH Q13 Continuous Manufacturing of Drug Substances and Drug Products
  - Supporting development and implementation for FRAME
- Workforce development
  - Provided training to support ETT graduation of continuous direct compression

Future Directions

- CDER Research Manufacturing Pilot Plant
  - Increase FDA's capability to generate knowledge and train FDA staff
- Continued investment in research programs for growing area in advanced manufacturing
  - Awarded five new collaborative projects in Sept. 2021
- Continued alignment of research programs to support ETP and development and implementation of FRAME

Product Development Science Program Summary

- Strengthens CDER's expertise in innovative technology
- Leverages external collaborations to enhance CDER internal capabilities
- Utilize new infrastructure for training of CDER and ORA staff in innovative technologies
- Aligns with the needs of ETP 2.0 and FRAME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