

# A Framework for Regulatory Advanced Manufacturing Evaluation

**Adam Fisher**

Associate Director of Science & Outreach  
Office of Pharmaceutical Quality  
CDER | US FDA

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# Learning Objectives

- Understand the **importance of advanced manufacturing** to American public health.
- Explain CDER's efforts to **develop a regulatory framework** that accommodates innovation.
- **Share progress** and discuss what is on the horizon.



# What is Advanced Manufacturing?

- Integrating **novel technological approaches**
- Using established techniques **in a new or innovative way**
- Applying production methods **in a new domain** where there are no defined best practices or experience



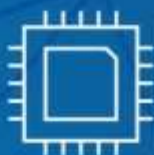
# The Current Landscape

- **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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ADMINISTRATION



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

# Getting Started

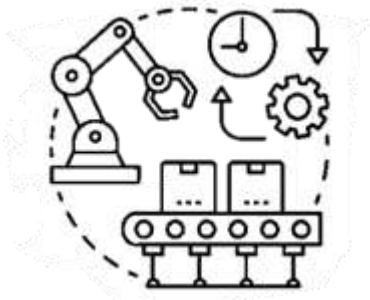


- Funded the National Academies to **gather public input** on emerging technologies.
- Described **Industry 4.0** and the future of pharmaceutical manufacturing

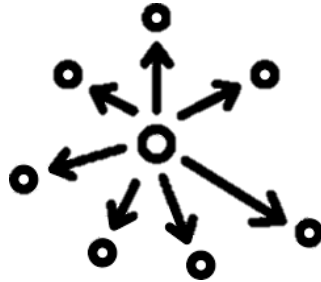


# Narrowing the Scope

**End to End Continuous  
Manufacturing (E2E CM)**



**Distributed  
Manufacturing (DM)**



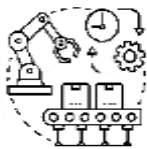
**Point of Care (POC)  
Manufacturing**



**Artificial  
Intelligence (AI)**



# AM Technologies

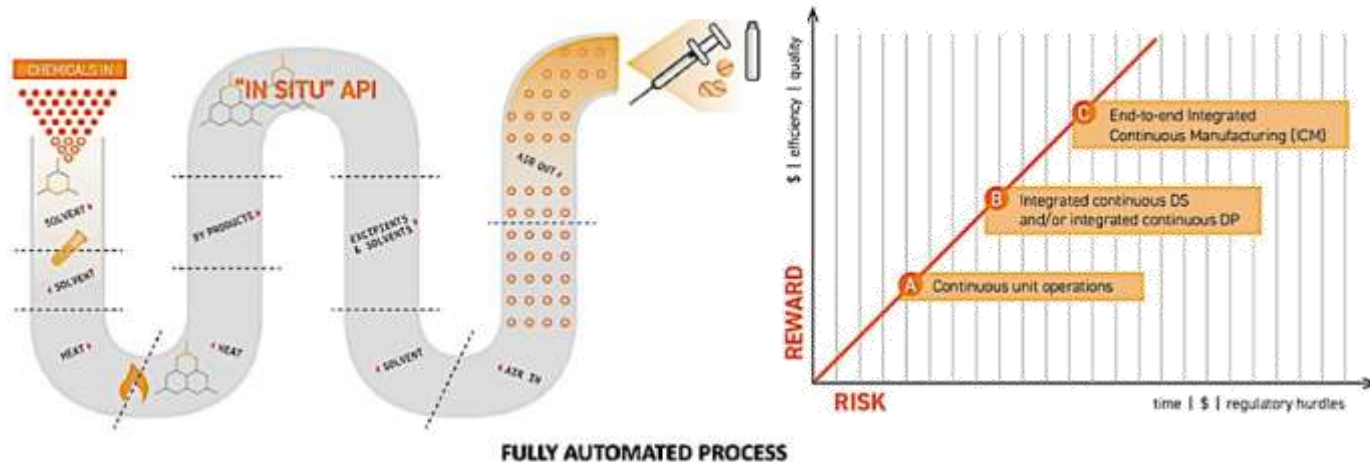


## End-to-End Continuous Manufacturing (E2E CM)

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.



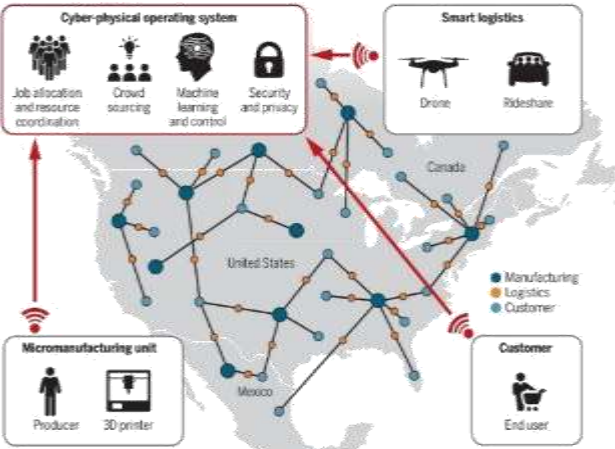
# End-to-End Continuous Manufacturing



Materials or chemical intermediates are **continuously fed into** and transformed within the system and finished drug products are **continuously removed** from the system

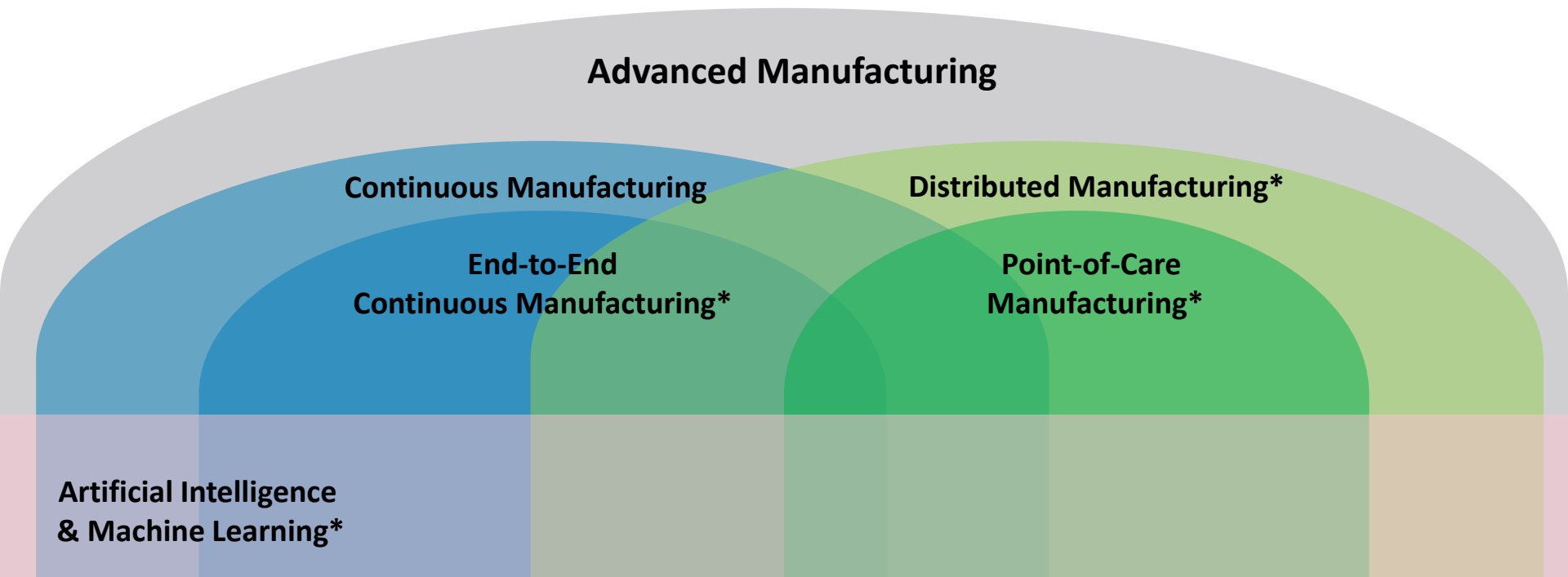


# Distributed Manufacturing



Platform is **decentralized and mobile**; it can be deployed to **multiple locations**, overseen and coordinated by a **single quality management system**.

# Ecosystem of AM Technologies



# Phased Approach to FRAME



## Phase I: Building the Foundation

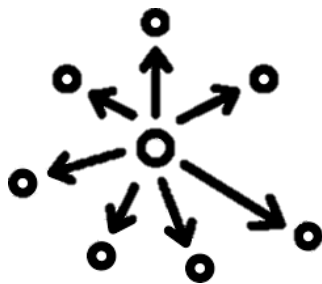
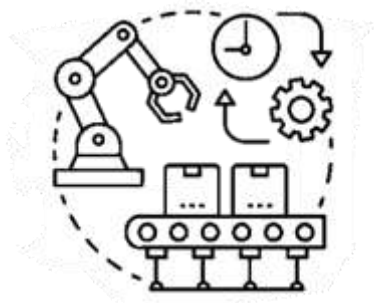
- Assessed existing guidance, regulations, and statutory authorities for **gaps and pain points**.



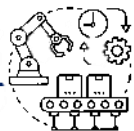
# Examples of Gaps and Pain Points



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

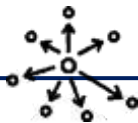


# Technology Gaps and Pain Points



## End-to-End Continuous Manufacturing (E2E CM)

- Covered by ICH Q13
- Not specific to E2E CM:
- Validation & Continuous Process Verification
- In-Process Controls



## Distributed Manufacturing (DM)

- Site Registration & Listing
- Post-Approval & Site Changes
- Regulation Conformance



## Point of Care (POC) Manufacturing

- Host Site Environment
- Central Control Site
- Inspection



## Artificial Intelligence (AI)

- Record Storage
- Big Data
- AI-Based Adaptive Control

## Phase II: Planning Implementation

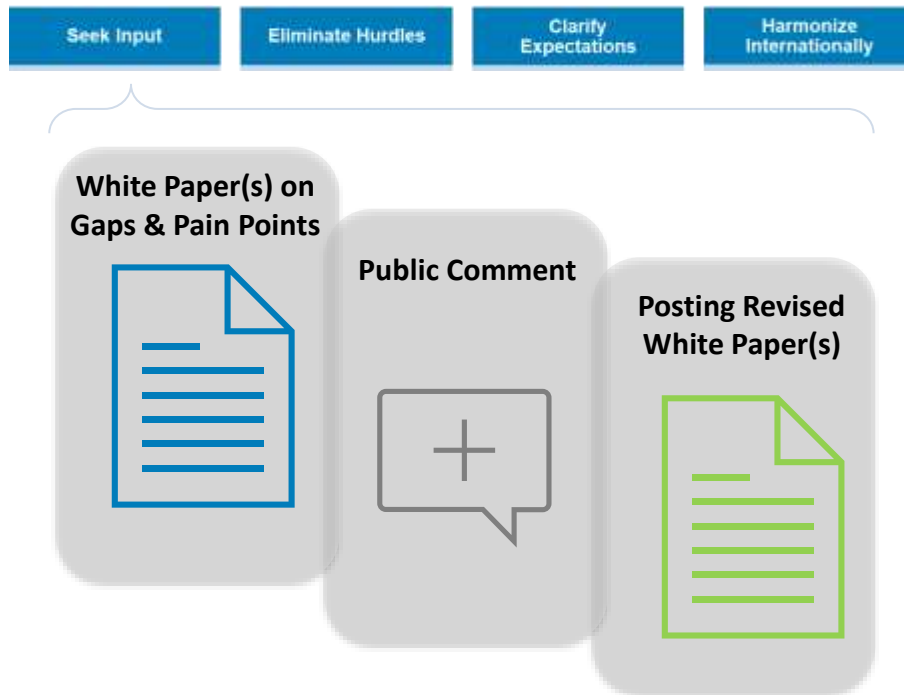
- Conducted in-depth impact analyses to make **recommendations for the regulatory framework.**



## 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.

### Phase 3 Priorities and Goals



# Summary



## 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.

# Challenge Question #1



**True or False:** Distributed Manufacturing (DM) is a decentralized, mobile manufacturing platform that can be deployed to multiple locations.

- A. True
- B. False

## Challenge Question #2

**True or False:** The planned regulatory framework is intended to only address current manufacturing innovation.

- A. True
- B. False