U.S. FOOD & DRUG ADMINISTRATION

Advanced Manufacturing and The Future of Pharmaceutical Quality

Michael Kopcha, Ph.D., R.Ph.
Director
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

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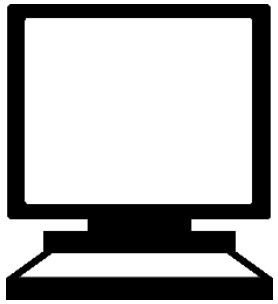
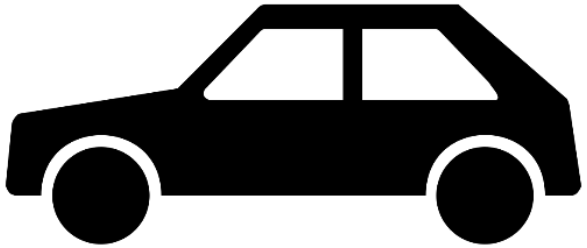
Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.





Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.

Patients expect safe and effective medicine with every dose they take

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects

It is what gives patients confidence in their *next* dose of medicine

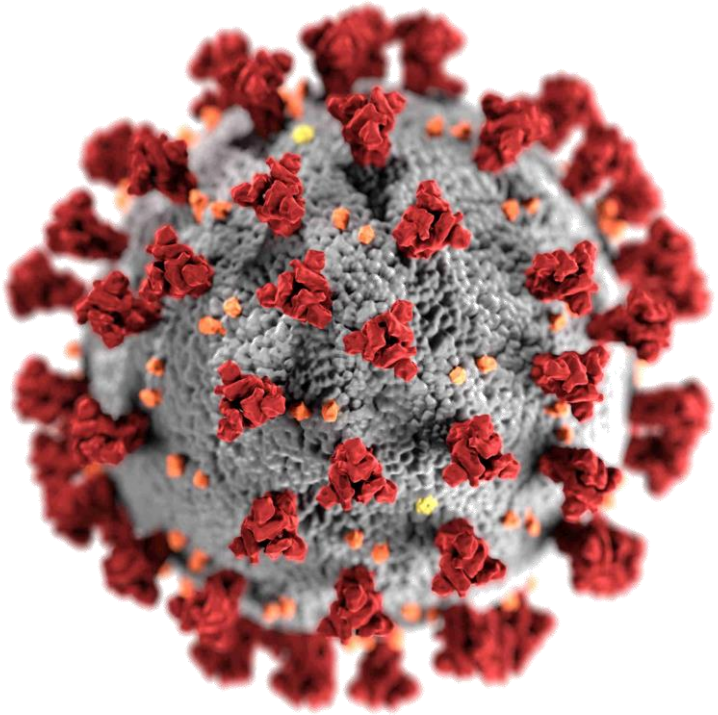
The Future of Pharmaceutical Quality

- Innovation in a Changing World
- Challenges and Opportunities
- The Importance of Advanced Manufacturing
- Regulatory Framework

Innovation in a Changing World

US FDA Center for Drug Evaluation and Research

The New Normal



A Vision of the Future

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Industry 4.0 for pharmaceutical manufacturing: Preparing for the smart factories of the future

N. Sarah Arden, Adam C. Fisher *, Katherine Tyner, Lawrence X. Yu, Sau L. Lee, Michael Kopcha

Food and Drug Administration, Center for Drug Evaluation and Research, Silver Spring, MD 20993, United States

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ABSTRACT

Over the last two centuries, medicines have evolved from crude herbal and botanical preparations into more complex manufacturing of sophisticated drug products and dosage forms. Along with the evolution of medicines, the manufacturing practices for their production have advanced from small-scale manual processing with simple tools to large-scale production as part of a trillion-dollar pharmaceutical industry. Today's pharmaceutical manufacturing technologies continue to evolve as the internet of things, artificial intelligence, robotics, and advanced computing begin to challenge the traditional approaches, practices, and business models for the manufacture of pharmaceuticals. The application of these technologies has the potential to dramatically increase the agility, efficiency, flexibility, and quality of the industrial production of medicines. How these technologies are deployed on the journey from data collection to the hallmark digital maturity of Industry 4.0 will define the next generation of pharmaceutical manufacturing. Acheiving the benefits of this future requires a vision for it and an understanding of the extant regulatory, technical, and logistical barriers to realising it.

1. Introduction

The term Industry 4.0 refers to the fourth industrial revolution which brings together rapidly evolving technologies such as the internet of things (IoT), artificial intelligence (AI), robotics, and advanced computing to dramatically change the landscape of manufacturing. Industry 4.0 is characterized by integrated, autonomous, and self-organizing production systems. New thinking will be required to realize Industry 4.0 for pharmaceuticals and overcome the inertia of current manufacturing infrastructure, operations, and regulation. While implementing many of the advanced technologies and manufacturing approaches needed to enable Industry 4.0 may not be easy, it may well be worthwhile as they bring the potential for higher output, increased manufacturing safety, improved quality, better value, increased agility, additional flexibility, and reduced waste (Ezell, 2016; Buvailo, 2018; Baur and Wee, 2015; Clemons, 2016; Tilley, 2017).

1.1. Industry 1.0

If Industry 4.0 is the future, then Industry 1.0 is the starting point of the modern pharmaceutical industry. The application of herbal or botanical preparations as medicines has spanned the history of civilization. Only in the last two centuries have we seen dramatic changes in how materials are processed and formulated for medical use. Industry 1.0 saw the manual processing of botanical, mineral, and animal derived materials transition from simple hand-operated tools to commercial-scale machinery able to crush, mill, blend, and press larger quantities of medicines (Anderson, 2005). In the 19th century, larger-scale production of drugs utilizing non-electrical power-driven machinery emerged from two sources – individual pharmacies or the dye and chemicals industry (Sonnedecker and Urdang, 1976; Daemmrich and Bowden, 2005). This movement from laboratory-scale to wholesale production of drugs fueled the establishment of a pharmaceuticals industry in the 19th century – an industry that has seen tremendous growth over the last century. Yet, some of the early machines from the first industrial revolution, such as pneumatic mills and tablet presses, are still commonly used today.

1.2. Industry 2.0

The second industrial revolution was enabled by electricity and early electronic machines and assembly lines with pre-set controls that

* Corresponding author at: Food and Drug Administration, Center for Drug Evaluation and Research, 10903 New Hampshire Ave, Silver Spring, MD 20993, United States.

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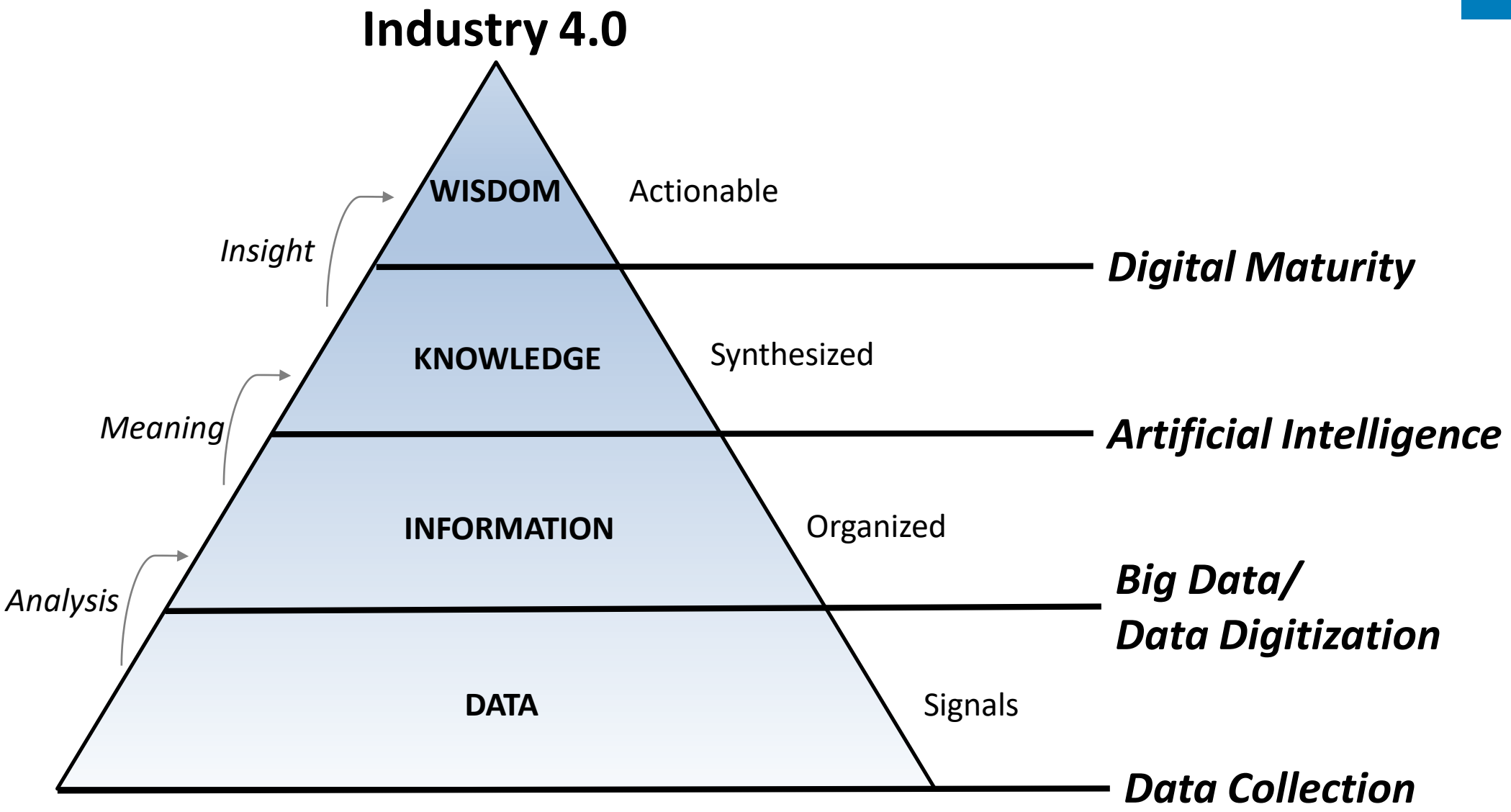
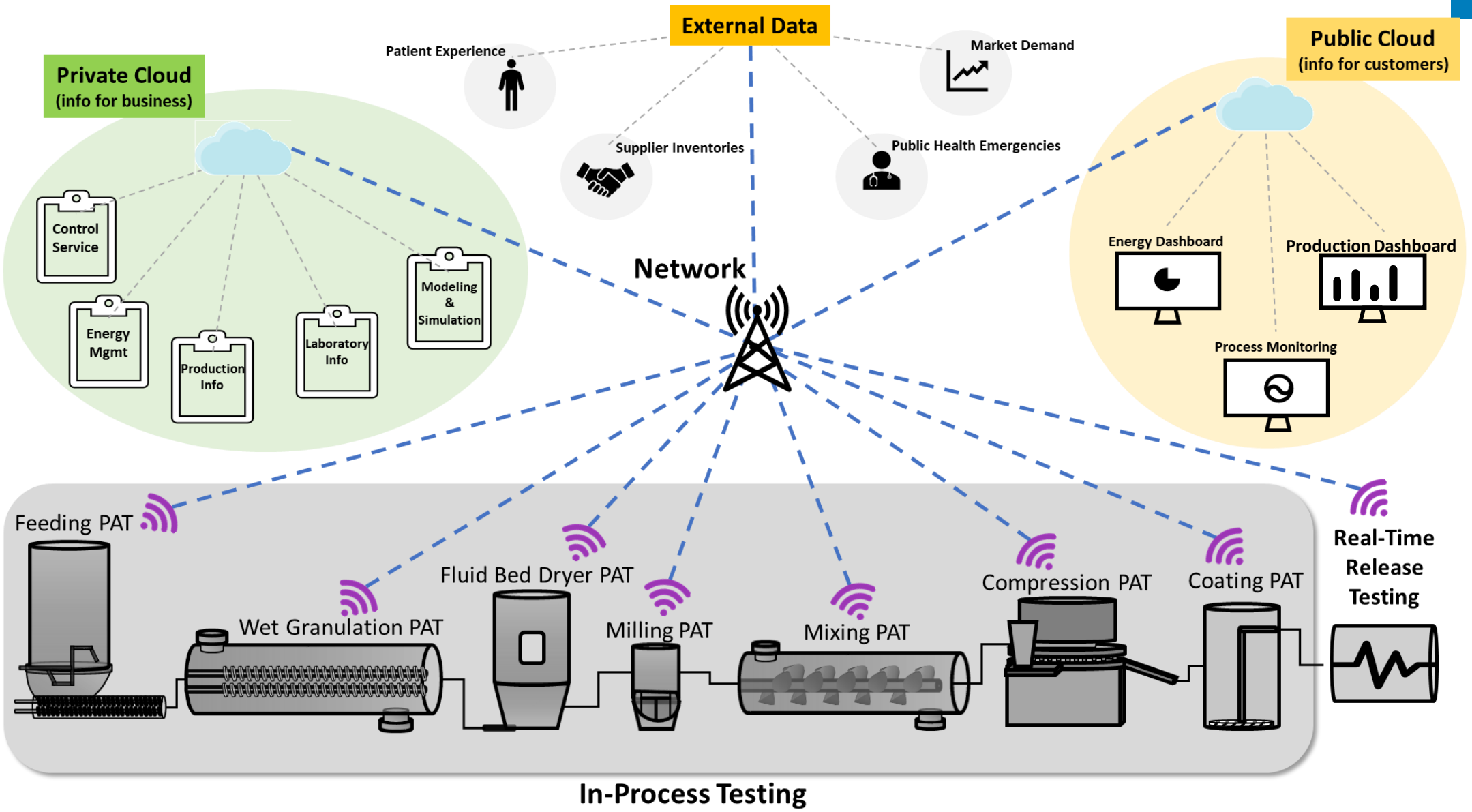
The Fourth Industrial Revolution in Pharma



The Fourth Industrial Revolution in Pharma



Challenges and Opportunities.

US FDA Center for Drug Evaluation and Research

The Three Pillars

Three pillars of a secure and robust supply chain are quality, diversification, and redundancy.

– 100-Day Report by

The White House

Challenge: Transparency

FDA should lead the development of a framework to measure and provide transparency regarding a facility's quality management maturity with engagement from industry, academia, and other stakeholders.

– 100-Day Report by

The White House

Challenge: Innovation

Advanced manufacturing offers many advantages over traditional pharmaceutical manufacturing, including that, once implemented, it can be used far more cost-effectively than traditional manufacturing.

– 100-Day Report by

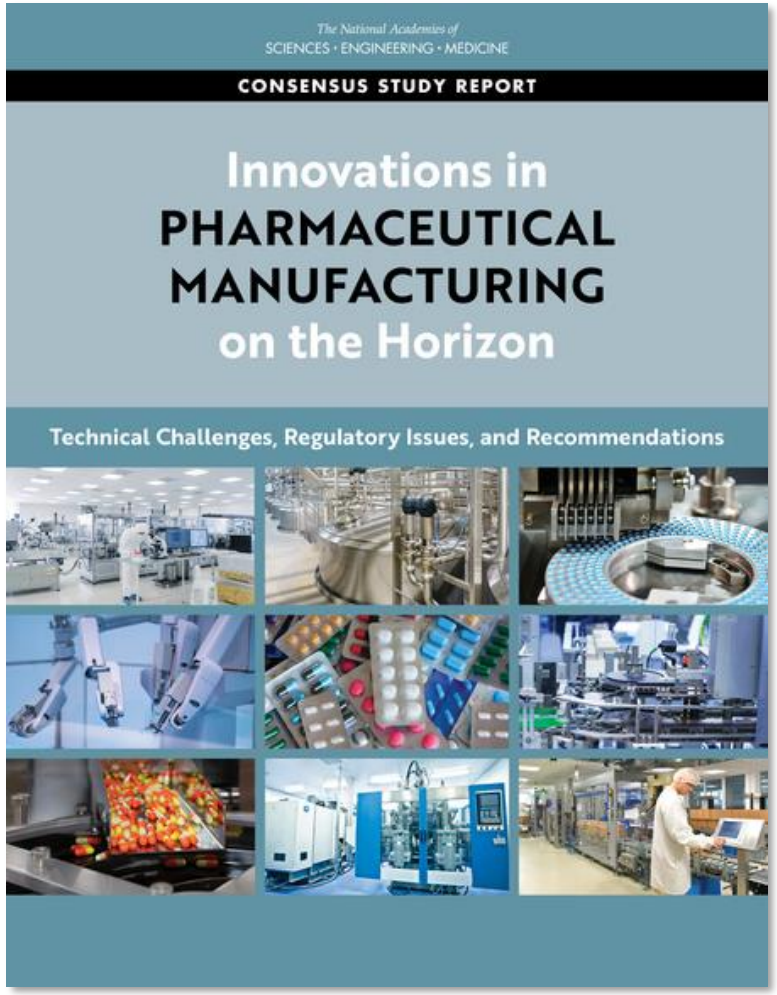
The White House

Advanced Manufacturing Benefits

Advanced manufacturing can improve manufacturing and ensure quality medicine is available.

- **Produce better quality medicine**. Facilitates six-sigma operation, no more than 3.4 defects per 1M opportunities.
- **Re-shore drug manufacturing facilities.** Helps domestic drug manufacturers compete in a global market.
- **Develop drugs rapidly.** Speeds the development of novel or patient-focused therapeutics.
- **Prevent drug shortages.** Reduces today's quality-related manufacturing issues causing 62% of drug shortages.
- **Improve emergency preparedness.** Provides more agility and flexibility to help pivot in a public health emergency.

Strengthening Our Expertise



The Importance of Advanced Manufacturing

US FDA Center for Drug Evaluation and Research

FDA's Advanced Manufacturing Initiatives

FDA's Advanced Manufacturing Initiatives Helping to Provide Quality Human Drugs for Patients

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Content current as of: 10/13/2021

Regulated Product(s): Drugs

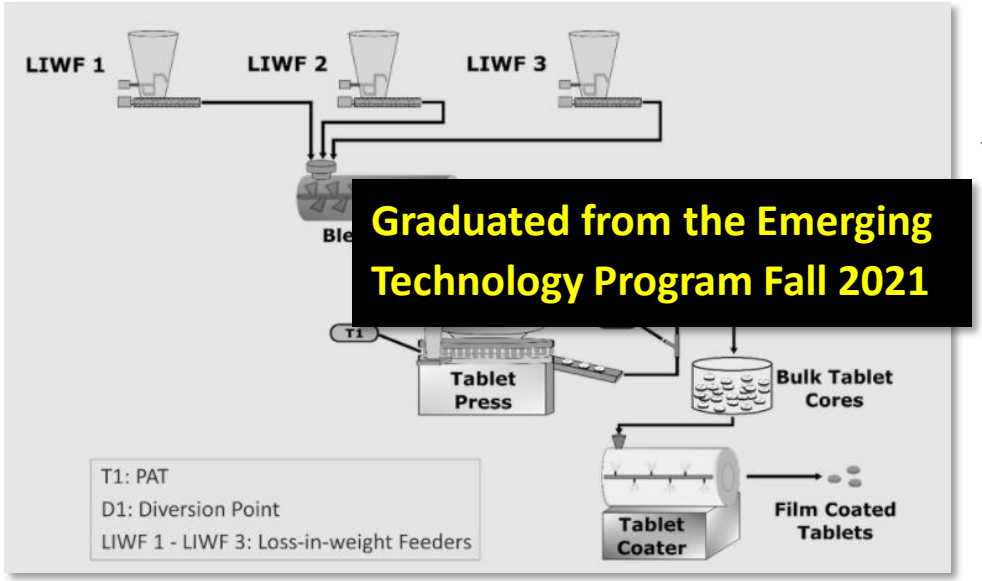
By: Michael Kopcha, PhD, RPh, Director of the Office of Pharmaceutical Quality (OPQ), Center for Drug Evaluation and Research (CDER) and Patrizia Cavazzoni, MD, Director of CDER

Part of this workshop:

- **Emerging Technology Program (ETP)**
- **Framework for Regulatory Advanced Manufacturing Evaluation (FRAME)**
- **Advanced Manufacturing Science & Research**

Emerging Technology Program

Continuous Direct Compression (CDC): ***a pharmaceutical manufacturing process that consists of dispensing materials, mixing them together, and compressing the blend to form tablets using integrated equipment with no breaks in the process.***



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

AM Science & Research

Continuous manufacturing of nanoparticles

End-to-end continuous manufacturing

Continuous bio-purification

Continuous direct compression

Continuous perfusion

3D Printing

High resolution mass spectrometry

In Closing

US FDA Center for Drug Evaluation and Research

Advancing Advanced Manufacturing

Advanced manufacturing is providing quality drugs to patients with cystic fibrosis, HIV, breast cancer, leukemia, and asthma.

Let’s *continue* working together to use innovation to handle an ever-changing world.


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