PDA COVID-19 Webinar Series – Utilization of Modular Manufacturing to Enhance/Upscale Capacity During COVID-19

September 23, 2020

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PDA COVID-19 Task Force Webinar Series

- As part of the ongoing work by the COVID-19 Task Force a series of webinars are being created.
- The webinars are focused on the COVID-19 pandemic and its current and future impact on pharmaceutical manufacturing.
- Some of the future webinar topics in the series will cover areas such as:
  - ✓ Performing remote supplier and internal audits with novel technology
  - ✓ Enabling change control flexibility in response to COVID-19
  - ✓ Environmental Controls for Coronaviruses in Pharmaceutical Manufacturing Facilities

Today's Webinar

General areas that will be covered:

- **An overview of the autonomous cleanroom system design and applications including:**
  - Comparison of traditional versus pre-fabricated offsite cleanroom construction.
  - Benefits of an autonomous cleanroom based facility approach. Specifically, as a response to the manufacturing needs as a result of the COVID-19 pandemic.
- **FDA stakeholder engagement activities related to prefabricated modular facilities.**
- **General understanding of the regulatory challenges related to the implementation of mobile manufacturing.**

Format for Today's Webinar

- After the introductions we will have presentations on autonomous cleanroom system design and its applications, and a regulatory perspective on advanced manufacturing and FDA's Emerging Technology Team.
- After which we will transition into a general Q and A discussion.
- The audience can submit questions throughout the webinar.

Niraj Mehta

Director, Chief of Staff, Global Quality Compliance (GQC), Merck

- Niraj leads the GQC Strategic Programs and Regulatory Intelligence team within Merck's Manufacturing Division. The team is responsible for the management of external policy and advocacy, and execution of processes to ensure Merck's Quality Compliance excellence.
- Prior to joining Merck, Niraj was a Pharmacologist within the Office of New Drugs and Office of Compliance within FDA's Center for Drug Evaluation and Research (CDER). His last role was within FDA's Office of Commissioner where he helped facilitate the adoption and implementation of the US-EU Mutual Recognition Agreement.

Dennis Powers

VP, Business Development & Sales Engineering,
G-CON Manufacturing

- Dennis has led G-CON's global business development activities since joining the company 7 years ago
- He has been the G-CON program lead for the PCMM collaboration with Pfizer since 2014
- Prior to joining G-CON, Dennis spent 20 years in the life sciences industry with Sartorius Stedim, Pall Danaher, and Precision Pharma Services in leadership roles across multiple functions including engineering, manufacturing, and validation.

Thomas O'Connor

Director Division of Product Quality Research, CDER's Office of Pharmaceutical Quality, FDA

- Tom's responsibilities include managing regulatory science projects to support the implementation of emerging technologies in pharmaceutical manufacturing such as continuous manufacturing, 3D printing, and the utilization of modeling and simulation for quality assurance.
- He is also a member of CDER's Emerging Technology Team (ETT) that provide a forum for firms to engage in early dialogue with FDA to support innovation and identifies and evaluates potential roadblocks relating to existing guidance, policy, or practice

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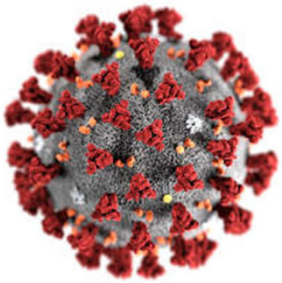
The Current State



- **The COVID-19 Pandemic has forced the industry to move with unprecedented speed to develop and commercialize a safe and effective vaccine**
  - Compress a development cycle that can sometimes take decades into just 12 months
  - Operation Warp Speed goal to deliver 300 million doses of safe effective vaccine by Jan 2021
- **Significant investment and efforts are well underway**
  - Over 100 vaccines and 250 therapies are being evaluated
  - 14 frontrunners, 5 selected by USG
  - Multiple vaccine types being developed
  - Potential for first supply of some vaccines to be available by end of 2020

The Manufacturing Challenge

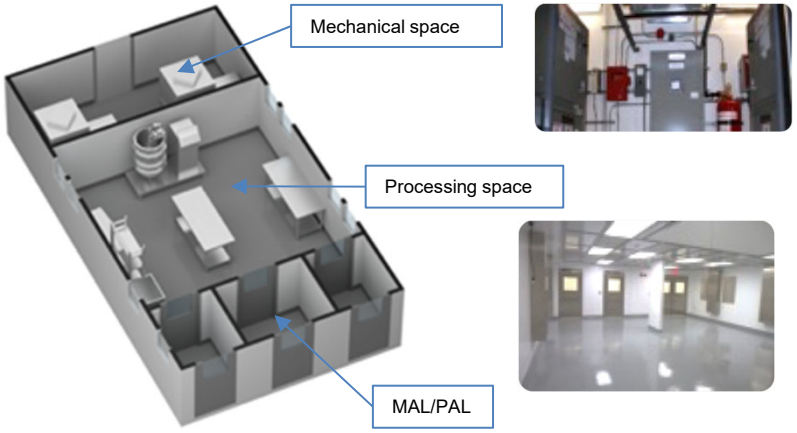
- **Every company with a potential candidate needs to be ready with capacity to produce vaccine at commercial scale**
  - Make vs Buy vs Partner
  - Different vaccine types have varying manufacturing processes, storage, and shipping conditions
  - Bulk drug and finished drug product capacity needed
  - Requires immediate investment in process and facilities at risk and accelerated execution
- **The pandemic has presented other challenges to drug manufacturers**
  - Maintaining operations and supply of existing products
  - Working with employee protective measures and restrictions
  - Resource availability to support other critical initiatives
  - Delays to current facility construction projects

How can we address the challenges?

- **First step – realize conventional thinking and methodologies will not work**
  - The acceleration of the design, construction, and validation of new cGMP drug manufacturing facilities requires innovative technologies and approaches
  - Utilization of pre-fabricated modular construction strategies including autonomous cleanrooms can be a potential solution
  - When combined with pre-engineered shell buildings and pre-fabricated utility skids, project schedules can be reduced significantly and with higher degree of certainty

What is an Autonomous Cleanroom?

- **A pre-fabricated cleanroom system that incorporates all structural, architectural, mechanical, electrical, and automation required for operation**
  - Factory built and tested prior to shipping
  - Rapidly installed, assembled and qualified in a new or existing shell building with available utilities
  - Cleanroom area can range from 500 SQFT to + 25,000 SQFT



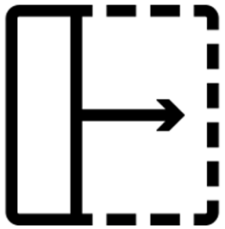
Comparison to Traditional Construction

	Stick-Built	Modular / Prefabricated Panels	Autonomous PODs
Cleanroom Image			
Decentralized HVAC	X	X	✓
Easily Scalable	X	X	✓
Easily Cloneable	X	X	✓
Mobile	X	X	✓
Delivery Time	2-3 years	1-3 years	3-10 months
Schedule Certainty	X	X	✓
Cost Certainty	X	X	✓

The Benefits of Autonomous Cleanrooms

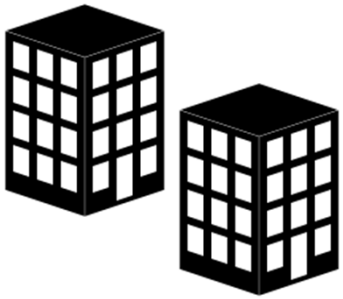
Direct impact to address COVID manufacturing challenges

Reduced Project Times



Scalability

Portable Platform



Clonability

Reduced Infrastructure Planning

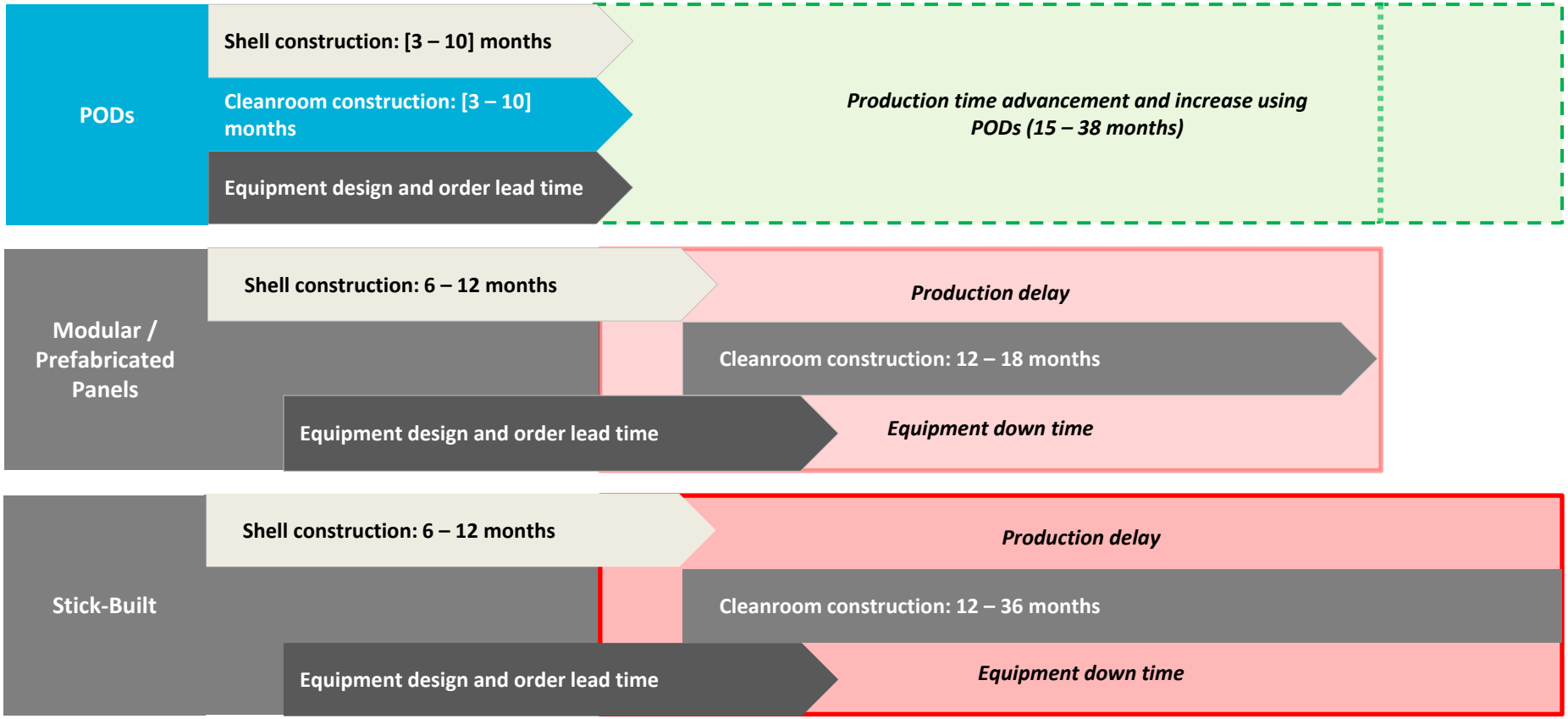
Value Increase

Equipment Integration

Robust Containment

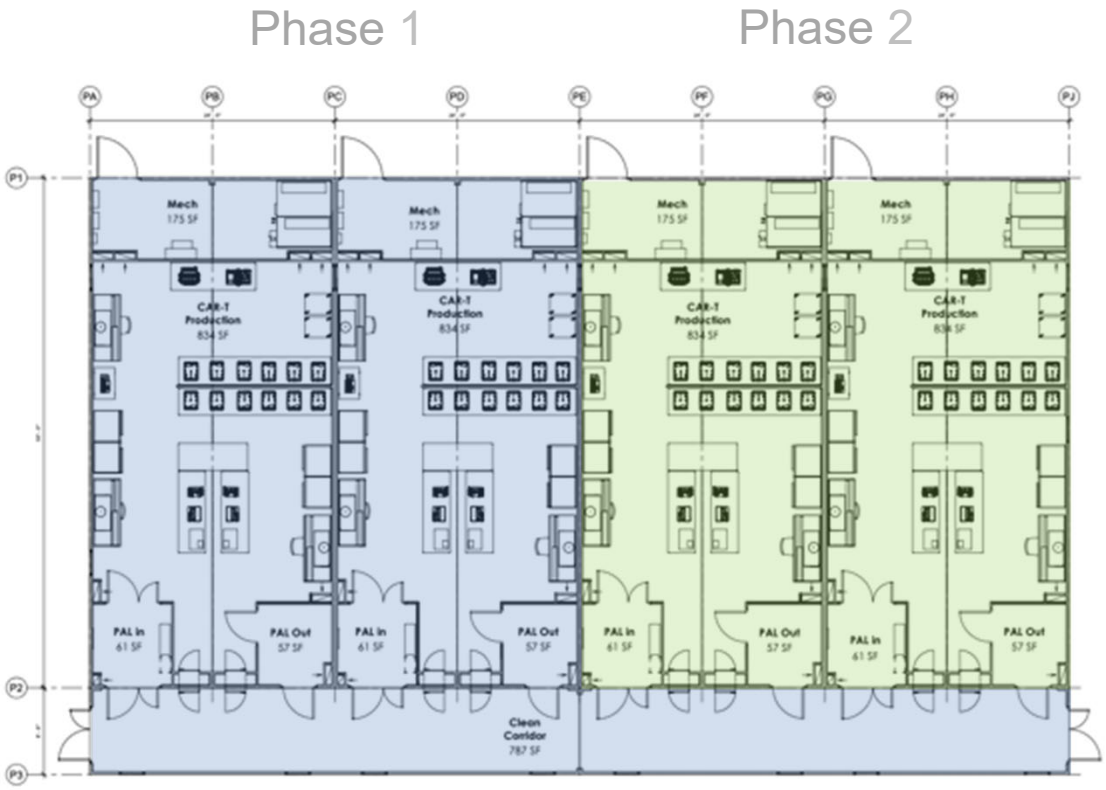
Benefit – Reduced Project Times

- **Pre-fabrication allows for faster construction and rapid installation**



Benefit - Scalability

- **Capacity increase and scalability with minimized interruption to existing processes**
  - Phased delivery to implement capacity as needed.
  - Opportunity to ramp capacity up or down as demand changes
  - Potential to continue operations or minimize downtime when additional PODs are installed



Benefit – Portable Platform

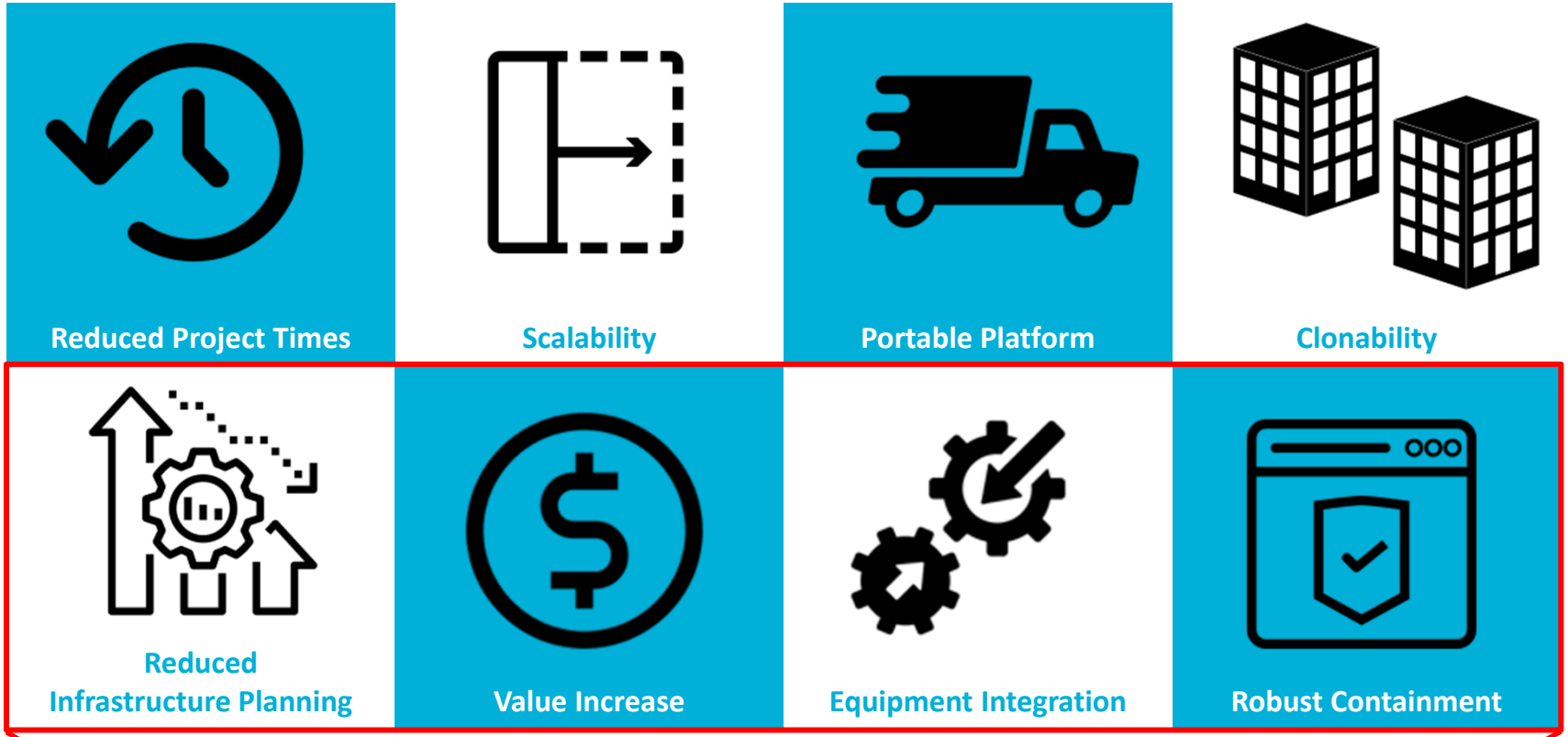
- PODs are mobile and can be transported around the globe due to robust aluminum superstructure
- PODs can be installed at ground level or on upper floor levels
- Airbearings integrated in floor structure allow for easy mobility within facility
- Installation in a facility can be permanent or PODs can be disassembled and relocated if needed
- PODs can be re-configured and re-purposed




Benefit – Clonability

- Engineering design time is significantly reduced
- PODs or a POD cluster can be cloned/copied to reduce the qualification time and regulatory burden.
- Allows staff of the new site being trained in the original site, reducing start-up delays
- Regulators inspecting the new site have an understanding and pre-knowledge since they know the original site

The Benefits of Autonomous Cleanrooms



FDA Perspective

Thomas O'Connor

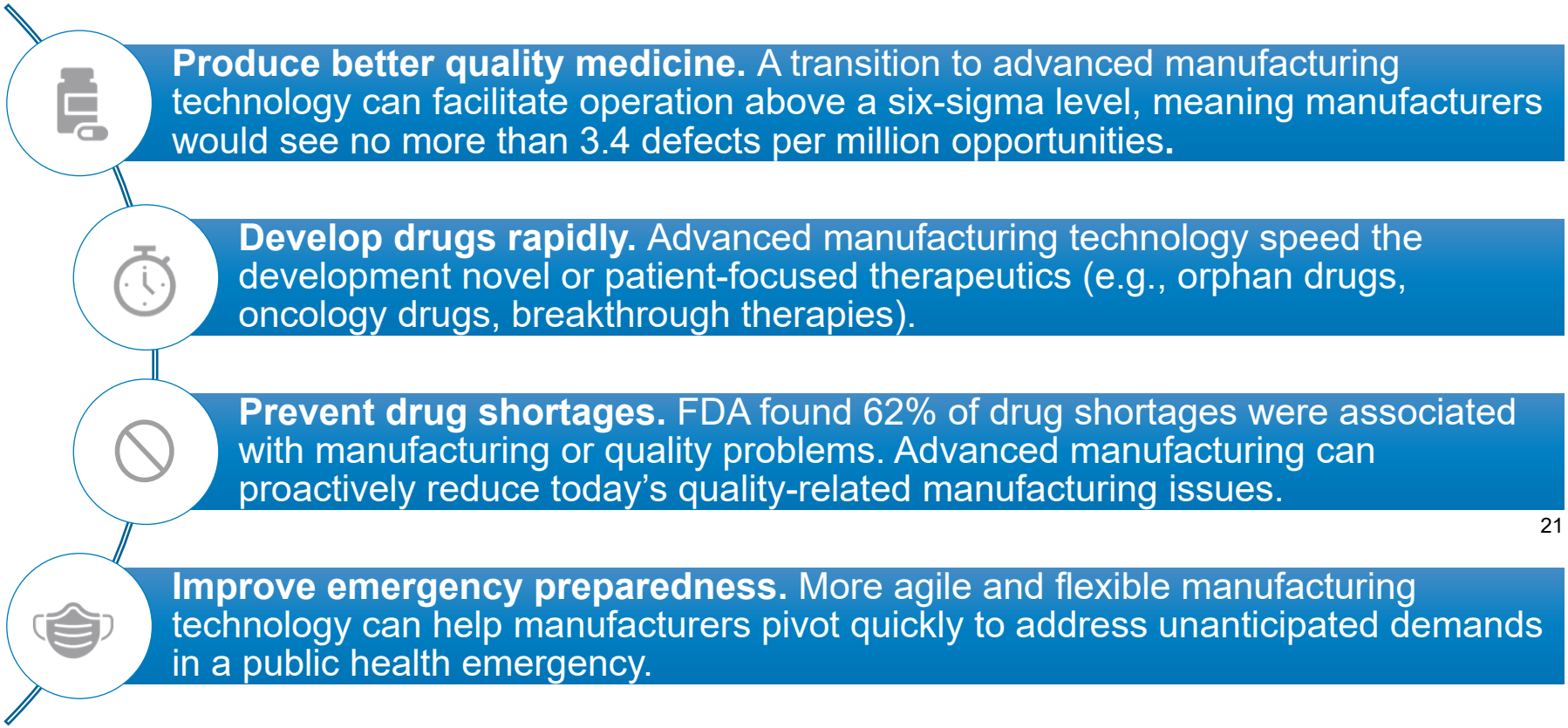
Director Division of Product Quality Research

CDER's Office of Pharmaceutical Quality, FDA

Advanced Manufacturing

Our vision is to achieve “a maximally efficient, agile, flexible pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight.” *Janet Woodcock MD, Director, CDER FDA*

Advanced manufacturing can improve drug manufacturing and help ensure that quality medicine is available.



Produce better quality medicine. A transition to advanced manufacturing technology can facilitate operation above a six-sigma level, meaning manufacturers would see no more than 3.4 defects per million opportunities.

Develop drugs rapidly. Advanced manufacturing technology speed the development novel or patient-focused therapeutics (e.g., orphan drugs, oncology drugs, breakthrough therapies).

Prevent drug shortages. FDA found 62% of drug shortages were associated with manufacturing or quality problems. Advanced manufacturing can proactively reduce today’s quality-related manufacturing issues.

Improve emergency preparedness. More agile and flexible manufacturing technology can help manufacturers pivot quickly to address unanticipated demands in a public health emergency.

CDER's Emerging Technology Team

Encourage and support the adoption of innovative technology to modernize pharmaceutical development and manufacturing through close collaboration with industry and other relevant stakeholders

CBER's Advanced Technologies Team (CATT)
Contact: Industry.Biologics@fda.hhs.gov

Program Objectives

To serve as a centralized location for external inquiries on novel technologies

To provide a forum for firms to engage in early dialogue with FDA to support innovation

To ensure consistency, continuity, and predictability in review and inspection

To engage international regulatory agencies to share learnings and approaches

To identify and evaluate potential roadblocks relating to existing guidance, policy, or practice

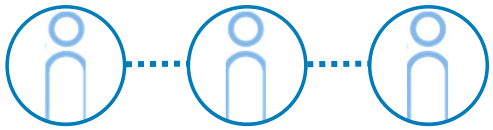
To facilitate knowledge transfer to relevant CDER and ORA review and inspection programs

To help establish scientific standards and policy, as needed

Contact us: CDER-ETT@fda.hhs.gov

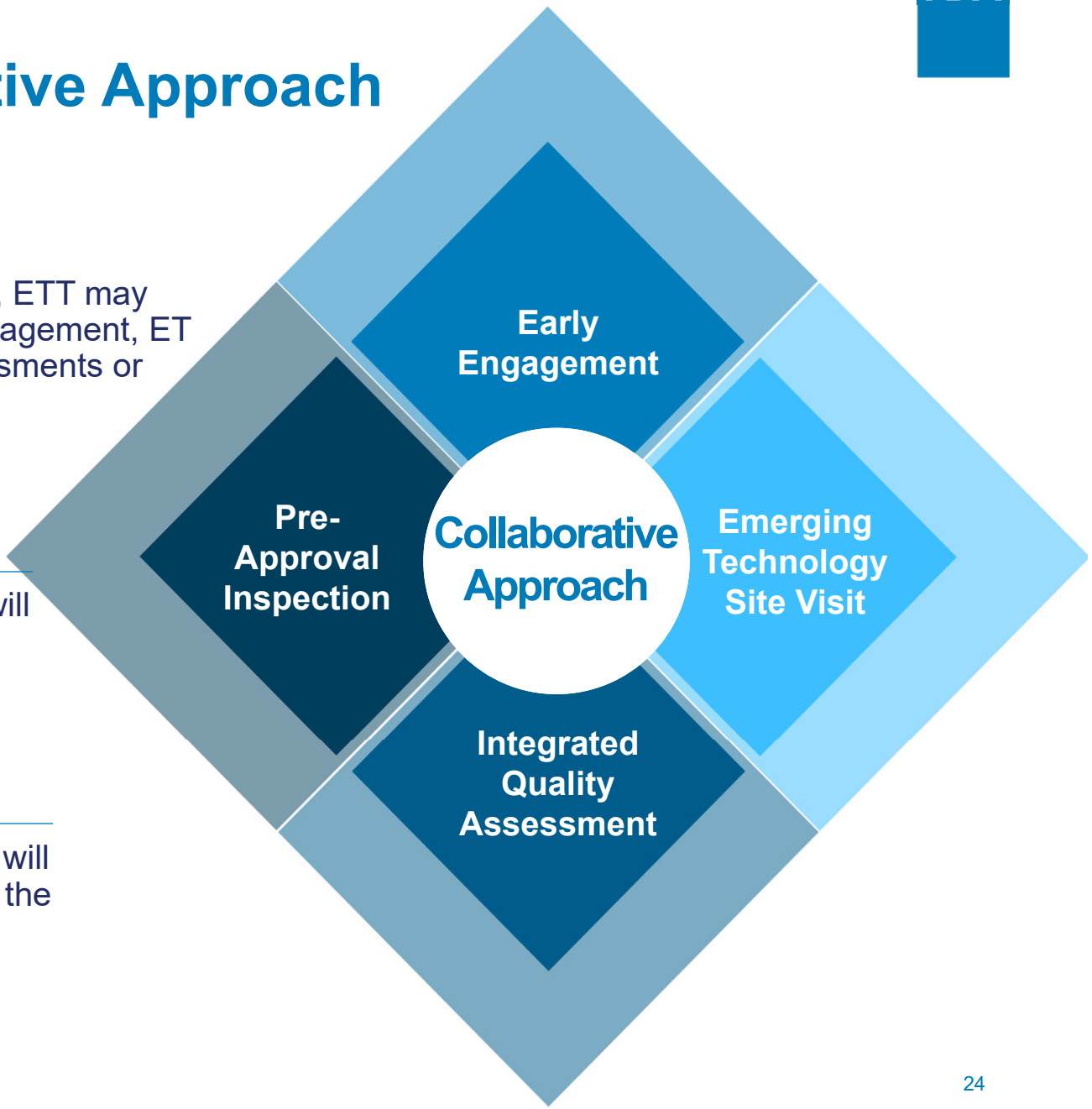
ETT Collaborative Approach

Over the course of an ETP project, ETT may employ a combination of early engagement, ET site visits, integrated quality assessments or Pre-Approval Inspections



The same ETT representative(s) will be involved in the entire process

The composition of a review team will likely remain the same throughout the entire process



Progress in Emerging Technology

Approval of a first regulatory application utilizing 3D printing technologies

Approvals of applications utilizing continuous manufacturing (CM)

- Small molecule drug product and drug substance
- Automated semi-continuous sterile manufacturing

Requests accepted to the ET program since launching in late 2014

- Received over 100 ETT proposals and accepted ~50% of these proposals to the program

Multiple submissions regarding the utilization of modular and mobile manufacturing facilities and processes

- Increase in engagement from different stakeholders during the pandemic

Use Cases for PODs Discussed with ETT

Expanding capacity at a given facility

- Implementing POD within existing facility

Mobile

- Relocating PODs between existing facilities

Cloning

- Replicating PODs to increase capacity

Response to Public Health

- Moving POD to point of care/ emergency response

Regulatory Considerations

- Depends on Use Case
- Considerations should be based on science and risk
  - Engaging with stakeholders to understand the impact of utilizing PODs on product quality risk factors
- Aligning PODs with current definition of establishment
- Impact on Quality Systems should be evaluated

Q&A
Please submit your questions!

Merry Christie

Product Quality Team Lead
CDER's Office of Pharmaceutical Quality, FDA

- Merry leads a team of CMC/product quality assessors in Office of biotechnology products (OBP) at FDA
- She is also a member of the CDER's Emerging Technology Team (ETT) and several FDA working groups, whose responsibilities include supporting the implementation of advanced manufacturing technology through collaboration with industry and evaluation of potential regulatory roadblocks to the implementation of such technologies
- She has14 years of combined experience in assessing CMC/product quality data and performing research to develop and advance pharmaceutical drug development

Brian Horman

Vice President, Facilities & Engineering
Just – Evotec Biologics

- Brian oversees design, construction and operation of labs, clinical and commercial facilities for Just – Evotec Biologics. He is currently managing a $100M+ project for drug substance production that is utilizing modular cleanrooms for the production areas for a bulk drug substance manufacturing plant. He also utilized modular cleanrooms for an earlier international manufacturing facility.

- Prior to joining Just in 2015 Brian was at Amgen/Immunex for 14 years. He oversaw multiple large projects domestically and internationally including labs, drug substance manufacturing, fill/finish, packaging & distribution facilities and campus development.

Laurie Norwood

President, Norwood Biologics Consulting LLC

- Laurie advises clients on regulatory pathways and GXP compliance required for the manufacture of biological drug products in all phases of the product life cycle. She provides clients support in facility design, control and prevention of cross contamination, regulatory submissions and quality system evaluations with an emphasis on novel cell and gene therapy and vaccine products.

- Prior to establishing Norwood Biologics, she served 33 years at the FDA. During her last 13 years at the FDA, she was Deputy Director for the Division of Manufacturing and Product Quality (DMPQ) in the Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research. Throughout her FDA career she was involved in the regulation of biological drug products and policy and development of guidance documents related to the review and inspection of products regulated by the FDA.

Thank You For Attending Today's Webinar

Our next PDA COVID-19 Task Force Webinar will focus on:

Remote Auditing Technologies

Tentatively Scheduled for: October 28, 2020

Stay informed of all PDA events at: PDA.org

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