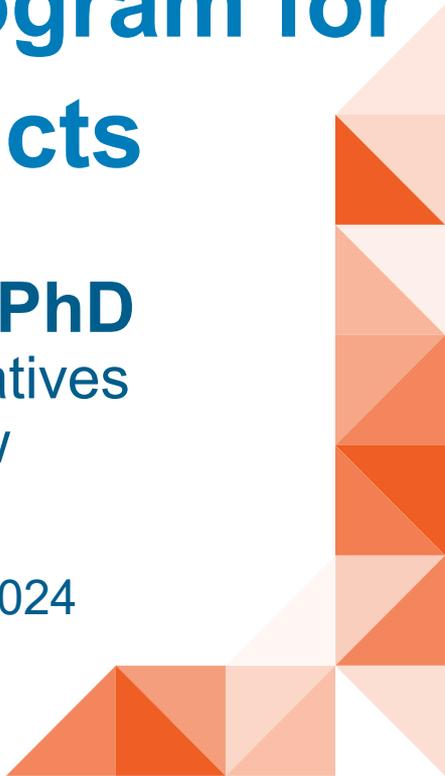


Advanced Manufacturing Program for CBER-Regulated Products

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Office of Vaccines Research and Review
CBER | US FDA

2024 Regulatory Education for Industry – May 30, 2024



Learning Objectives

- To understand the framework and approach for on Advanced Manufacturing Program for CBER-Regulated Products.

Informal Communication Disclaimer



My comments are an informal communication and represent my own best judgement. These comments do not bind or obligate FDA.

About Advanced Manufacturing for Public Health Emergency Preparedness and Response

Advanced manufacturing can help rapidly scale manufacturing capabilities, increase supply chain resilience, and provide new tools to address drug shortages

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An FDA researcher completes a 3D print of several clinical and research tools for patient-specific medicine (FDA photo)

Content current as of:
12/13/2023

Topic(s)
Research

[About Advanced Manufacturing for Public Health Emergency Preparedness and Response | FDA](#)

fda.gov/cdersbia

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
- Every field has a different set of production techniques that are considered advanced



[About Advanced Manufacturing for Public Health Emergency Preparedness and Response | FDA](#)

Benefits of Advanced Manufacturing

- Improve drug quality
- Strengthen domestic drug supply
- Prevent drug shortages due to quality-related issues (majority of drug shortages)
- Expedite drug development and speed time to market
- Greater agility and resilience in responding to public health emergency

Biological Products Regulated by CBER



Blood, blood components and derivatives

Vaccines (preventive and therapeutic)

Tissues

Cell and gene therapies

Xenotransplantation

Allergens

Related devices (including IVDs)

CBER Advanced Technologies Program



Fund advanced research and development projects to support regulatory science and innovation



Build internal scientific and regulatory expertise



The CBER Advanced Technologies Team (CATT)

CBER Advanced Technologies Team (CATT)



WHAT

Established in 2019 to promote dialogue, education, and input among CBER staff and between CBER and prospective developers of advanced manufacturing technologies to encourage their implementation in the manufacturing sector.

WHO

Consists of a small cross-functional group representing CBER leadership, relevant policy, review and inspection programs.

Offices Represented: OD, OVRR, OTP, OBRR, OCBQ

HOW

Provides access to early interactions with CBER, prior to filing a regulatory submission, to discuss technical and regulatory issues related to the implementation of innovative manufacturing and control strategies .

Early Engagement with CBER



Non-binding regulatory advice

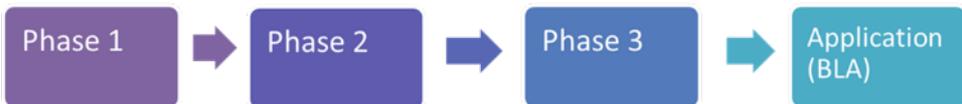
CATT Interaction

- CMC
- Innovative approaches to product development

INTERACT Meeting:
Specific product and indication for first-in-human use

- CMC
- Pharm/tox
- Clinical

Binding regulatory advice



• Pre-IND Meeting:

- Manufacturing
- Lot Release
- Animal safety & immunogenicity
- Phase 1 protocol

IND = Investigational New Drug
BLA = Biologics License Application
NDA = New Drug Application

• EOP 2 meeting:

- Phase 3 protocol(s)
- Phase 1 & Phase 2 data
- Animal efficacy protocols & data (if “Animal Rule” used)
- Update on manufacturing & lot release

• Pre-BLA/NDA Meeting:

- Clinical data summary: Safety & Efficacy data
- Manufacturing, etc...
- Outline of BLA/NDA

Advancing Innovative Manufacturing Technologies through Extramural Funding



Since 2018 CBER has awarded several grants and contracts to support research projects to study improvements for advanced manufacturing of biological products



Funded research addresses knowledge and experience gaps identified for emerging manufacturing and testing technologies and support the development and adoption of such technologies in the biological product sector

Examples of Supported Projects

- 3D Bioprinting for tissue engineering
- Novel manufacturing approaches for cell therapy products (CQA discovery, purification, continuous production)
- Continuous Manufacturing (Vaccines, AAV vectors for gene therapy)
- Process modeling/simulation
- Non-destructive analytics (NMR) for evaluating product quality

<https://www.fda.gov/vaccines-blood-biologics/industry-biologics/cber-advanced-technologies-program-extramural-research-funding>

Scope of CATT Meetings



Novel technologies with significant impact on product development, manufacturing process and control strategies

Manufacturing and analytical methods for which CBER has **limited experience**

Not for product-specific, highly technical discussions



Submitting CATT Meeting Requests

<https://www.fda.gov/vaccines-blood-biologics/industry-biologics/cber-advanced-technologies-team-catt>

A 2-page (including figures and tables) backgrounder that provides the following information:

- Description of **technology**
- Why technology/product class is **novel and unique**
- **Impact** of technology/product class
- Summary of **manufacturing or development plan**
- **Questions** regarding perceived regulatory, technical, or other challenges for implementation

Review Process



Evaluation:

- Initial triage by CATT coordinators
- Assignment to relevant Review Office(s)
- Discussion at recurrent internal CATT meetings

Review Process



Possible Outcomes:

- CATT meeting granted
- Provide responses to submitted questions
- Recommendation to request other meetings for product-specific discussions

Examples of Technologies Discussed



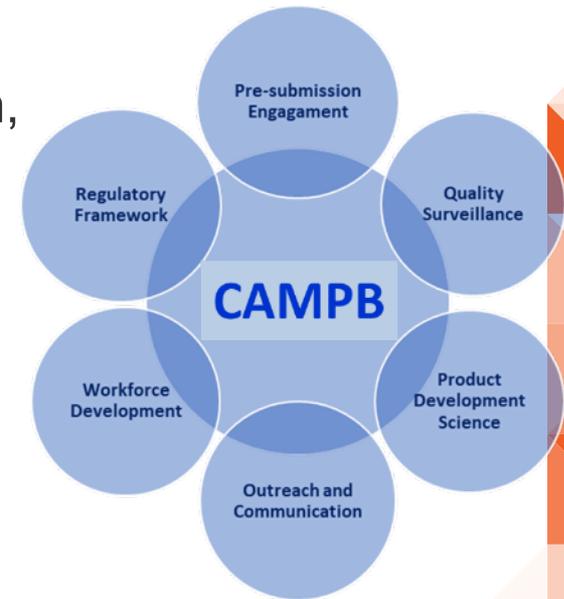
- Continuous Manufacturing (vaccines, AAV vectors, exosomes)
- Fully closed, automated, scalable and remote-controlled systems for manufacturing cell therapy products
- Improved cell lines for vaccine antigen production and AAV vector manufacturing
- Use of AI and advanced imaging technologies for real time product quality assessment
- Multi-product manufacturing facility design
- CRISPR/Cas9 Genome editing

CENTER FOR THE ADVANCEMENT OF MANUFACTURING PHARMACEUTICALS AND BIOPHARMACEUTICALS (CAMPB)



CAMPB Mission:

- Accelerate the development, implementation, and evaluation of advanced manufacturing by establishing science- and risk-based standards and policies
- Advance drug product development science
- Train a world-leading regulatory workforce, through strategic partnership, engagement and communication



FDA/PQRI AI Workshop



Virtual Event



PQRI **FDA** U.S. FOOD & DRUG ADMINISTRATION
Product Quality Research Institute

FDA/PQRI Workshop on the Regulatory Framework for the Utilization of Artificial Intelligence in Pharmaceutical Manufacturing

An Opportunity for Stakeholder Engagement

WORKSHOP OBJECTIVES

This FDA/PQRI Workshop will bring together leaders from regulatory agencies, industry, and academia to discuss critical topics related to the use of artificial intelligence (AI) in pharmaceutical manufacturing.

The National Academies of Sciences, Engineering, and Medicine (NAEM) noted that FDA is likely to see substantial innovations in pharmaceutical manufacturing which may impact process measurement, modeling, and control. AI technologies represent an area of rapid technology growth for designing, monitoring, and controlling manufacturing processes. Such AI technologies may challenge traditional approaches to regulating pharmaceutical manufacturing.

This workshop aims to facilitate interaction among AI stakeholders on critical areas for development, implementation, and regulatory consideration including uses in process development and control, operation of Pharmaceutical Quality Systems, lifecycle approaches, and Current Good Manufacturing Practice.

The FDA recently published a [discussion paper](#) on this topic in the Federal Register and the comment period ended on May 1, 2023.

PQRI encourages anyone interested in utilizing AI technologies in pharmaceutical manufacturing to register for this workshop and join the discussion.

REGISTRATION IS OPEN.
CLICK [HERE](#) TO REGISTER

TUES. - WED.
SEPT. 26-27, 2023

VIRTUAL WORKSHOP

10 AM - 3 PM
each day

+1 (202) 230-5607
PQRIsecretariat@pqri.org

Stay up to date by visiting the Workshop Website at:
<https://pqri.org/fda-pqri-aiworkshop/>

www.pqri.org

<https://pqri.org/fda-pqri-aiworkshop/>



ICHQ13: Continuous Manufacturing of Drug Substances and Drug Products

Objective

Provide harmonized guidance for the development, implementation, and assessment of continuous manufacturing (CM) technologies used in the manufacture of drug substances and drug products

Scope

Applies to CM of chemical entities and therapeutic proteins, and the conversion of batch manufacturing to CM for existing products. ICH Q13 principles may also apply to other biological/biotechnological entities.

About the Advanced Manufacturing Technologies Designation Draft Guidance

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/advanced-manufacturing-technologies-designation-program>

AMTD Draft Guidance contains information on:



- The **process** for **submitting** an AMT designation request
- Description of **eligibility criteria**
- **Data and information** to be included in the designation request
- **When and how FDA will communicate receipt** of and **determination** for an AMT designation request
- **When and how FDA will assess AMT designation requests**
- The **process** by which FDA will **engage** with holders of designated AMTs and applicants
- **Benefits of the Program**

Summary



- CBER is committed to accelerating the **adoption** of advanced manufacturing technologies - **CATP**
- CBER encourages innovators to engage the Center early to discuss regulatory and technical issues associated with innovative technology implementation - **CATT**
- CBER is collaborating internally and internationally to build the scientific expertise and regulatory framework necessary to evaluate emerging technologies

CAMPB, FRAME, ICH Q13

Challenge Question #1



Which of the following best fits description of Advanced Manufacturing :

- A. Use established techniques efficiently
- B. Use established techniques effectively
- C. Use established techniques in a new or innovative way
- D. Substitute established techniques using other techniques

Challenge Question #2



Which of the following is an example of Advanced manufacturing?

- A. Manufacturing of Drug Substance and Drug Products in a GMP facility
- B. Use of Continuous Manufacturing (Vaccines, AAV vectors for gene therapy)
- C. NMR for advanced research
- D. 2D Bioprinting

Thank you!

Sudhakar Agnihothram

Sudhakar.Agnihothram@fda.hhs.gov

<https://www.fda.gov/vaccines-blood-biologics/industry-biologics/cber-advanced-technologies-program>

