U.S. FOOD & DRUG ADMINISTRATION

Facilitating Advanced Technologies in Cell and Gene Therapies

CGTP 2021 Virtual
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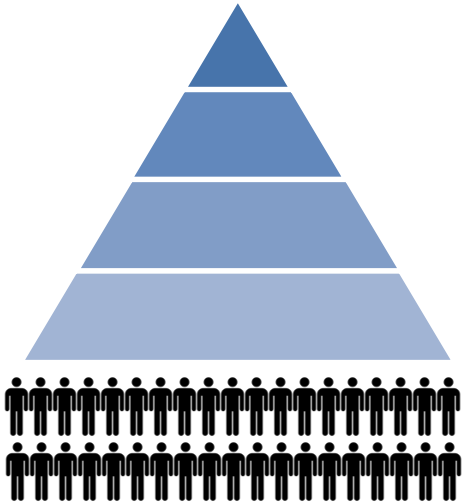
Different manufacturing paradigm

Conventional Drug/Biologic

1 product lot



Many patients

Unique issues for CGT products

Advanced manufacturing

Advanced QC technologies

Scale up/scale out

Comparability

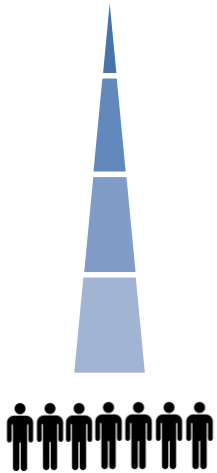
Raw materials

Distribution

Impact of manufacturing failure

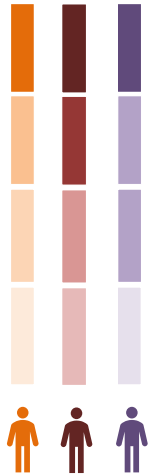
Cell & Gene Therapy Products

1 product lot



Few patients

1 product lot



Single patient

Advanced Manufacturing?

A collective term for new medical product manufacturing technologies that can improve drug quality, address shortages of medicines, and speed time-to-market. Every field has a different set of production techniques that are considered advanced. It often:

- Integrates novel technological approaches
- Uses established techniques in a new or innovative way, or
- Applies production methods in a new domain where there are no defined best practices or experience.

https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing

Why Advanced Manufacturing?

- CGT products may require complex manufacturing processes. Advanced manufacturing may bring new tools to address:
  - Flexibility
  - Availability
  - Scalability
  - Cost

- What do we mean by advanced manufacturing?

  Innovative technologies such as:
  - 3D bioprinting
  - Continuous manufacturing
  - Cell culture systems supporting large scale or rapid production
  - Monitoring/measurement technologies
  - Bioinformatics pipeline

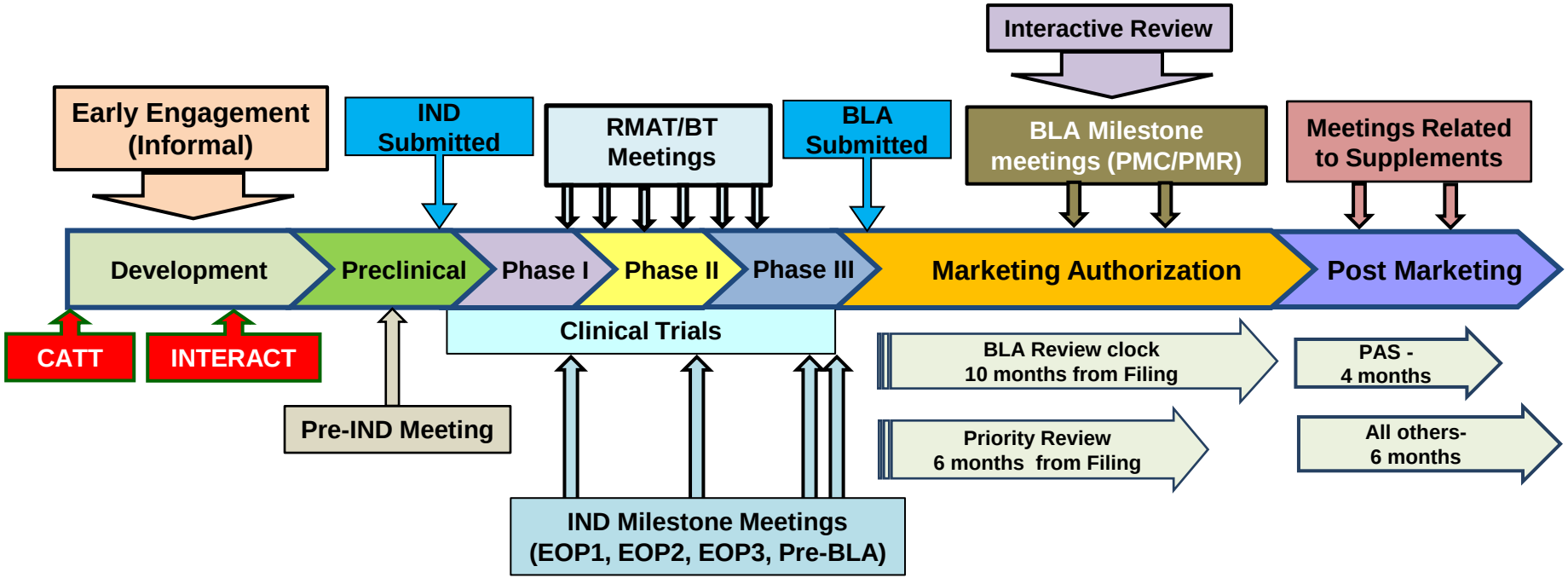
CBER Initiatives to Promote Development of Advanced Manufacturing Technologies

CBER Advanced Technologies Program:

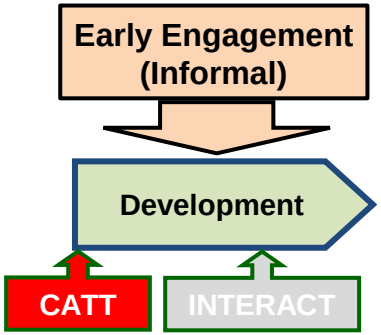
- CBER Advanced Technology Team (CATT)
- Build internal scientific and regulatory expertise
- Promote the creation of more modern Domestic Manufacturing

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

Interaction with CBER/OTAT



CBER Advanced Technology Team (CATT)



- Provides an interactive mechanism to prospective developers of novel therapies to discuss the implementation of the needed technologies in the development of CBER-regulated biologics products
- Allows access to early interactions on more general topics before filing of a regulatory submission
- Scope of inquiries or meeting requests:

  Innovative approaches to biologic product development such as
  - Novel technologies that can have a significant impact on product development
  - Manufacturing process and control strategies with potential regulatory implications
    - Manufacturing and analytical methods for those products or classes of products for which the center has limited experience with the manufacturing or development process
- CBER participants:
  - CBER management, relevant Office management and review staff

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

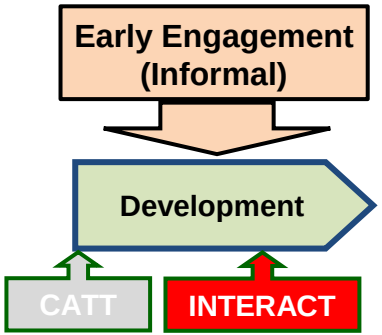
CATT Inquiries and Meeting Requests

- Submit requests electronically to Industry.Biologics@fda.hhs.gov and include CATT in the subject line

- Include the following information (two pages including figures and tables):
  a. Brief description of the technology or product class
  b. Brief explanation why the technology or product class is substantially novel and unique
  c. Description of the impact of the technology or product class in terms of improved biologic product manufacturing, characterization, quality, safety, or efficacy
  d. Summary of the manufacturing or development plan and any questions regarding perceived regulatory, technical, or other challenges for implementation

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

INTERACT



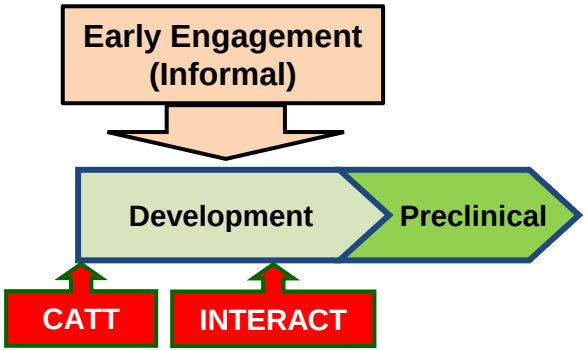
- **INTERACT: INitial Targeted Engagement for Regulatory Advice on CBER producTs**
- INTERACT Meetings Program was created for potential sponsors to engage with CBER staff and obtain advice on a specific topic or issue that is critical to early product development
- Development of innovative investigational products have unique challenges
  - complex manufacturing technologies and issues
  - use of cutting-edge testing methodologies
  - unknown safety profiles
  - incorporation of innovative devices

INTERACT Meetings

- CMC: Issues and testing strategies to demonstrate product safety, adequate to support a first-in-human study
- Pharm/Tox: Design of proof-of-concept or other pilot safety/biodistribution studies necessary to support administration of an investigational product in a first-in-human clinical trial
- Clinical: General recommendations regarding a future first-in-human trial in a target clinical population.
- All requests received via general CBER email: INTERACT@fda.hhs.gov
- SOPP 8214: INTERACT Meetings with Sponsors for Drugs and Biological Products

https://www.fda.gov/BiologicsBloodVaccines/ResourcesforYou/Industry/ucm611501.htm

Early Engagement via CATT and INTERACT



CATT Interaction:

- Innovative approaches to product development
- CMC

INTERACT Meeting:

Specific product and indication for first-in-human use

- CMC
- Pharm/tox
- Clinical

CBER Initiatives to Promote Development of Advanced Manufacturing Technologies

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Building Internal Scientific and Regulatory Expertise

- Develop and support CBER research programs to improve understanding of advanced manufacturing for vaccines and cell and gene-based therapies
  - Hiring of new principal investigators (PIs) to develop research projects and regulatory expertise
  - Hiring of new full-time reviewers

- CBER Advanced Technologies Seminar Series
  - CBER hosts academia/industry experts in advanced manufacturing technologies

Promote the creation of more modern Domestic Manufacturing

- 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 Grants awarded (FY18-present)

Carnegie-Mellon University: Addressing key manufacturing needs for extracellular matrix scaffold 3D printing

Georgia Institute of Technology: Data enabled automation for the improved efficacy, yield and reproducibility of the manufacturing of mesenchymal stromal cells for clinical therapeutic use

Harvard University: Antigen-presenting cell mimetic scaffolds for expansion of higher quality therapeutic T-cells

Massachusetts Institute of Technology: Continuous viral vector manufacturing cased on mechanistic modeling and novel process analytics

Massachusetts Institute of Technology: Flexible Platform for End-to-end Manufacturing of Gene Therapies to Advance the Development of Treatments for Ultra-rare Diseases

Rutgers University: Develop and implement a platform technology-based testbed of a fully automated and integrated continuous upstream bioprocess

https://www.fda.gov/news-events/fda-brief/fda-brief-fda-awards-grants-foster-innovation-advanced-manufacturing-technology-part-agencys-efforts

Examples of Contracts Awarded (FY19-present)

Draper Laboratory: Continuous Acoustic separation for therapeutic cell manufacturing

General Electric Global Research Center: Simplified and agile AAV production by integrating rapid DNA synthesis with continuous AAV collection

Georgia Institute of Technology: Identification of critical quality attributes of cell therapy products by multi-omics analyses and predictive modeling

Southwest Research Institute: Evaluate the Safety and Quality of a 3D Printed, Single-Use Bioreactor for Beads-Free CART T-cell Manufacturing

University of Maryland: Nondestructive analytics for vaccines

Path Toward Progress

- Keep pace with advancing technology
- Refine regulatory framework as necessary
- Overcome limitations in manufacturing
- Collaborate nationally and internationally
- Facilitate optimal product development

Contact information

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- **Regulatory Questions:**

  OTAT Main Line – 240 402 8190
  Email: OTATRPMS@fda.hhs.gov and
  Lori.Tull@fda.hhs.gov

FDA Headquarters

- **OTAT Learn Webinar Series:**
  http://www.fda.gov/BiologicsBloodVaccines/NewsEvents/ucm232821.htm
- **CBER website:** www.fda.gov/BiologicsBloodVaccines/default.htm

  Phone: 1-800-835-4709 or 240-402-8010

- **Consumer Affairs Branch**: ocod@fda.hhs.gov
- **Manufacturers Assistance and Technical Training Branch**: industry.biologics@fda.gov
- **Follow us on Twitter:** https://www.twitter.com/fdacber


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