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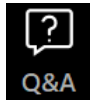
Accelerating CMC Readiness for Selected Drug and Biologic Applications

Wednesday, May 15, 2024, 1:00PM (ET)

The Webinar Will Begin Shortly



- **Questions?** Please **type your questions into the Q&A box** in your Zoom control panel for our speakers.
- **Post-webinar?** A recording of this webinar will be available for future viewing of the presentation.
- **Feedback?** A survey will be available at the conclusion of the webinar. We welcome your comments!

Speakers & Moderators

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FDA Pilot Overview

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CDRP Webinar
Cosponsored by FDA, BIO & PhRMA
05/15/2024

Chemistry, Manufacturing, and Controls (CMC) Development and Readiness Pilot (CDRP) Program

Ingrid Markovic, Ph.D.
Senior Science Advisor
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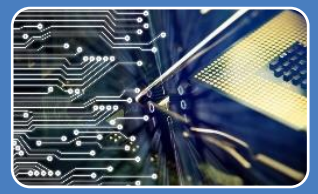
PDUFA VII Novelty

First time CMC is part of the PDUFA negotiations since program inception in 1992

PDUFA VII: CMC Commitments

Enhancing Communication Between FDA and Sponsors During Application Review (i.e., 4-Part Harmony)



Advancing utilization and implementation of innovative manufacturing

Considering alternative tools to assess manufacturing facilities

Enhancing Inspection Communication for Applications

CMC Development & Readiness Pilot (CDRP) Program

Why the Webinar?

Through this webinar we aim to share information about the CDRP program including clarifying any ambiguities and explaining the benefits of the program with a goal to boost pilot participation and address any questions or concerns that potential participants may have.

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CMC Development and Readiness Pilot (CDRP) Program Origin

CDRP Program Origin: Why is it needed?

Industry expressed concerns that CMC has become a bottleneck for the premarket review of expedited products

FDA observed gaps in the CMC information in expedited applications, which may suggest that CMC development is not progressing at the same pace as clinical development

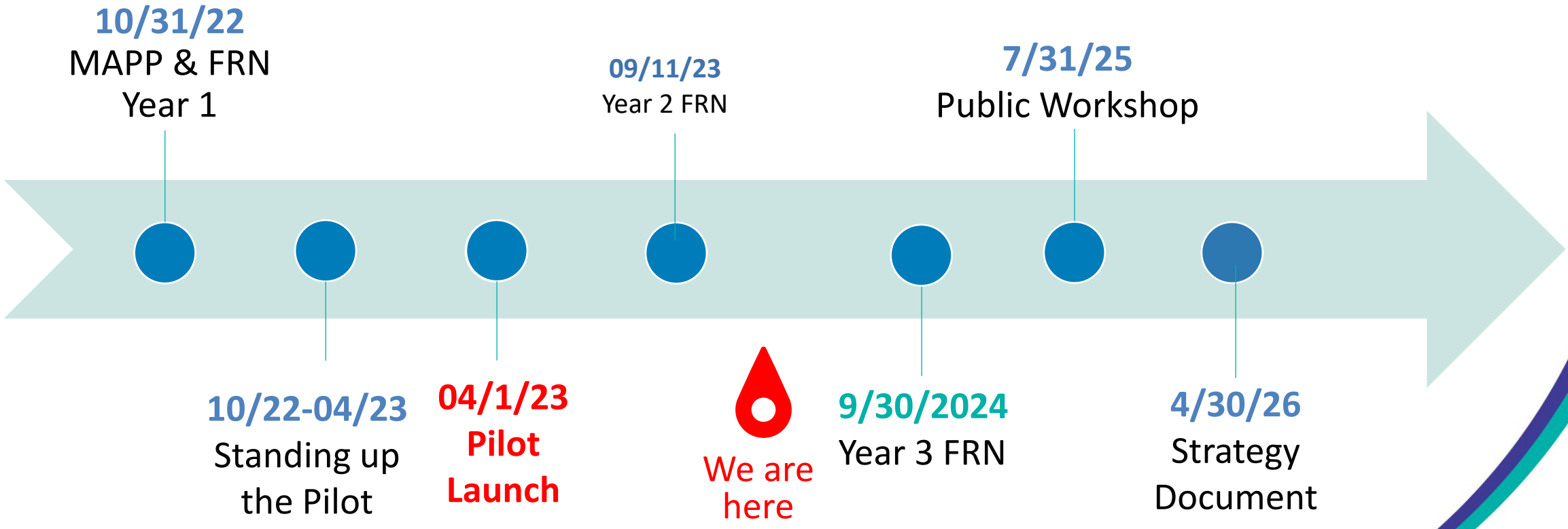
Sponsors with expedited programs would benefit from a proactive focus on CMC activities early on. This, coupled with additional guidance from the FDA would help ensure that CMC can keep pace with clinical dev. mitigating delays and better aligning overall product development

CMC Development and Readiness Pilot

PDUFA VII CDRP commitment:

Starting in FY 2023, FDA (CDER and CBER) will conduct a CMC Development and Readiness Pilot (CDRP) to facilitate the expedited CMC development of products under an IND application based upon the anticipated clinical benefit of earlier patient access to the products. The goal of the Pilot will be to facilitate CMC readiness for CBER- and CDER-regulated products with accelerated clinical development timelines.

CDRP Commitment Timeline



Currently, all deliverables are on target to meet PDUFA VII Commitment dates

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CDRP Program: Anticipated Benefits

CDRP Program: Anticipated benefits

- **Early Access: Provide patients with earlier access to transformative therapies**
- **Time to Market**: Speed time to market
- **Data Supporting Approval: Mitigate knowledge gaps**
  - ✓Identifying CMC areas that require attention can help de-risk future manufacturing, but also through increased knowledge, identify opportunities for improvement and optimization (cornerstone of QRM)
- **Application Process:** More complete CMC application package reducing burden on the FDA & Applicant
  - ✓More first cycle approvals
  - ✓Fewer Major Amendments
  - ✓Fewer IRs
  - ✓Facility readiness

CDRP Program: Anticipated benefits (cont.)

- **Meet Market Demand:** Ensure robust supply once product is approved
- **Resources:** De-risk resource expenditure
  - Manufacturing readiness could help identify ways to streamline operations and increase productivity as well as mitigate the need for additional studies which may help reduce the overall cost of production
- **Innovation**: Promote innovation and shared understanding in this area through best practices and lessons learned presented in a public workshop as case studies.

Early Interaction with FDA Could Help Address CMC Challenges

- **Scale up/scale out and Tech Transfer in preparation for commercial launch**
  - ✓ Challenges with transitioning from small-scale operations to commercial-scale production, and effectively transferring the process to commercial site
- Proactive planning for **manufacturing process changes** and **comparability assessment**
  - ✓ Mitigate last minute manufacturing changes requiring comparability assessment and possibly additional studies if unable to demonstrate comparability
- **Commercial process validation** ensuring manufacturing consistency
- **Designing control strategy**
- **Analytical method** design, development, and validation
  - ✓ Potency assay development for biological products
- **Stability studies** (stability study design and challenges with completing stability studies)
  - ✓ Understanding when predictive modeling can be helpful
- **Bioinformatics**, reference standards, level of data gathered, and unique aspects of each platform

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CDRP Program: Main Features

CDRP: What to expect?

- **Two dedicated CMC meetings** (Type B meetings, in addition to existing meetings)
  - To provide guidance on CMC readiness and address specific CMC questions and challenges
- **Follow-up discussions** (to address questions arising from the meeting or meeting minutes)

Type B Meetings Under CDRP

- FDA will follow Type B meeting timelines (will be scheduled within 60 days of the request (see FDA Guidance: Formal Meetings between FDA & Sponsors or Applicants)
- In the meeting request
  - ✓Submit questions
  - ✓When feasible, recommend submitting a meeting package with the meeting request
- Sponsors can request the meeting format
  - ✓Written response
  - ✓Teleconference
  - ✓Face-to-face (in person or virtual)

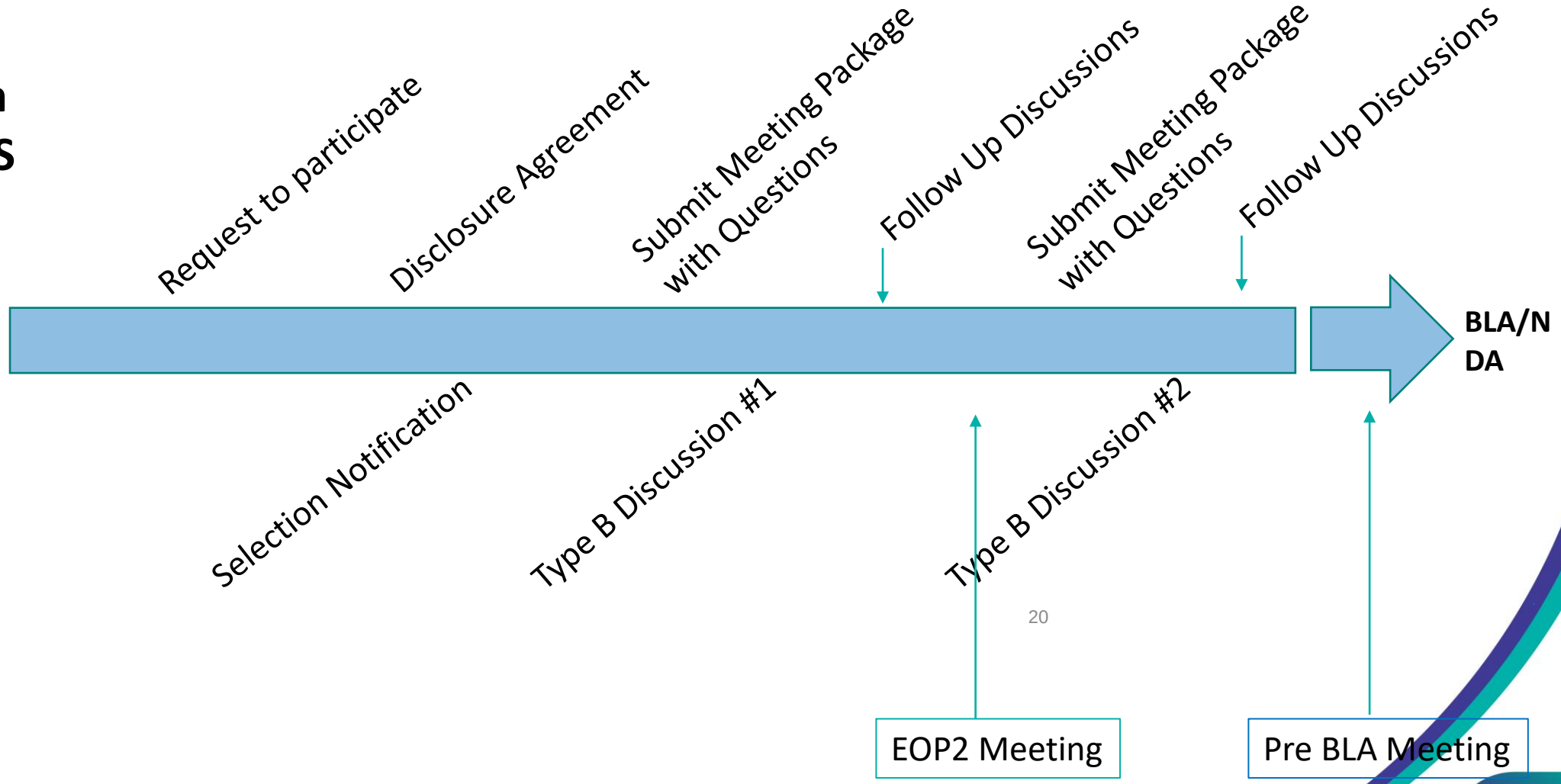
Follow up Discussions

- Follow up discussions* may be in the form of
  - ✓Teleconference
  - ✓Written response
- Sponsors should send a written request with Questions in an amendment to the IND
  - ✓Cover letter should mention CDRP in the subject line
  - ✓Request should include background information related to the questions with reference to the previous FDA communication

* Follow-up discussions are for questions arising outside Type B meetings

An example of CDRP Process Flow

CDRP Program INTERACTIONS



*CDER will consider INDs without a formal designation

Program Capacity

- FDA will select no more than 9 proposals per fiscal year over a 4-year period starting from April 2023-2027
  - Approx. 6 CBER and 3 CDER (Note: this is flexible and depends on how many applications each Center receives and resources available)

CDRP Eligibility and Selection Criteria

Joint CBER and CDER Eligibility Criteria

- An active commercial IND
- eCTD format, unless a waiver is granted
- In general, at the time of submission, the IND has not reached the end of Phase 2. Exceptions could be considered (see FRN).
- Combination products (21 CFR 3.2 (e)(1)) are eligible
- A plan to pursue CMC development that aligns with the expedited clinical development timeframe

CBER-Specific Eligibility Criteria

- An existing **CBER-regulated IND** intended for submission as an BLA for:
  - ✓Cellular Therapies
  - ✓Gene Therapies
  - ✓Other products regulated by CBER Office of Therapeutic Products
  - ✓Vaccines regulated by CBER Office of Vaccines Research and Review
- IND has a Breakthrough Therapy (BT) or Regenerative Medicine Advanced Therapy (RMAT) designation.

CDER-Specific Eligibility Criteria

- An existing **CDER-regulated IND** intended for submission as an NDA or BLA
- **Products with expedited clinical timeframe**
  - A Breakthrough Therapy (BT), or Fast Track (FT) designation,
  - Other products that have an expedited clinical timeframe based upon the anticipated clinical benefits, with their eligibility to be determined by FDA
    - ✓ CDER will consider INDs without a formal designation

Request to Participate and CMC Development Plan

Request to Participate

- Submit a written request to participate as an **Amendment to the IND** to the appropriate center (CBER or CDER)
- Include IND number and expedited program designation (e.g., FT, BT, RMAT) as well as the date designation was granted

Information to Include in a Request to Participate in the CDRP Pilot

- Current state of CMC development
- Projected timelines for CMC development that aligns with clinical development
- CMC Development Plan (see next slide)
- Any known and/or anticipated CMC challenges
- If known, proposed timing for the first CMC-specific Type B meeting

CMC Development Plan

- **Map out a plan for manufacturing readiness highlighting potential challenges (if known)**
- Available product characterization and critical quality attributes
- Description of drug substance and drug product manufacturing process and control strategy (bioassays, as applicable)
- Plan for proposed commercial scale manufacturing and control strategy
- Manufacturing facilities and inspection history
- Plans to ensure product availability for commercial launch
- Drug substance and drug product stability plan
- Process validation plans

Selection Process

- Review occurs quarterly (or as needed)
- FDA is targeting to notify the Sponsors about selection within 180 days of receipt
- Selection Criteria:
  - Whether facilitating earlier patient access would be clinically beneficial
  - Novelty or complexity of the product, manufacturing process or technology

Balance and diversity in product types, sponsors, therapeutic indications

CDRP Disclosure Agreement

Disclosure Agreement

- **FDA will continue to ensure confidentiality of submitted information**
  - ✓**Only information that is discussed and agreed upon between applicant & FDA will be disclosed**
- Information shared may include generalized and anonymized product-agnostic case studies
  - ✓Broadly applicable strategies that could help streamline CMC development
- A disclosure agreement (DA) letter will be sent to the sponsors prior to final selection in the pilot
  - ✓The DA template will include examples of the type of information that will be disclosed
  - ✓DA language may be subject to negotiation

Workshop and Strategy Document

Workshop and Strategy Document

FDA will conduct public workshop towards the later part of PDUFA VII period

- Goal: To promote innovation and develop shared understanding about CMC readiness
- IND Sponsors or FDA may present best practices and lessons learned as case studies during workshop
- FDA will issue a strategy document based on the experience from the pilot and workshop

Summary

- **Goal:** ***provide patients with earlier access to new drugs and biologics***
- The Pilot aims to facilitate CMC readiness for products with expedited clinical development timelines while maintaining Quality and Safety standards
- Increase communication between FDA and sponsors
- CDRP started April 2023 and sponsors are invited to apply
- Approximately 9 Applications will be accepted per year during the pilot – approx. 6 CBER and 3 CDER

Resources

- PDUFA VII Commitment Letter https://www.fda.gov/media/151712/download
- Federal Register: Chemistry, Manufacturing, and Controls Development and Readiness Pilot Program; Program Announcement
- FDA Guidance for Industry, Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD specifications https://www.fda.gov/media/135373/download
- Expedited Programs for Serious Conditions – Drugs and Biologics (https://www.fda.gov/regulatory-information/search-fda-guidance-documents/expedited-programs-serious-conditions-drugs-and-biologics)
- CDER MAPP 5015.13: https://www.fda.gov/media/162786/download
- CBER SOPP 8212.3: Management of Breakthrough Therapy-Designated Products: Sponsor Interactions and Status Assessment Including Rescinding (February 2022).
- CBER SOPP 8101: Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products (February 2022)

Q&A

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Closing Remarks

Thank you all for attending!