

CMC Development and Readiness Pilot (CDRP) Program

Regulatory Education for Industry (REdI)- 2023 Annual Conference

June 8-9, 2023

FDA, Silver Spring, Maryland

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Outline Of The Talk

Introduction

- Increase in INDs
- Breakthrough Therapy/Regenerative Medicine Advanced Therapy (BT/RMAT) Designations
- Compressed product development timelines

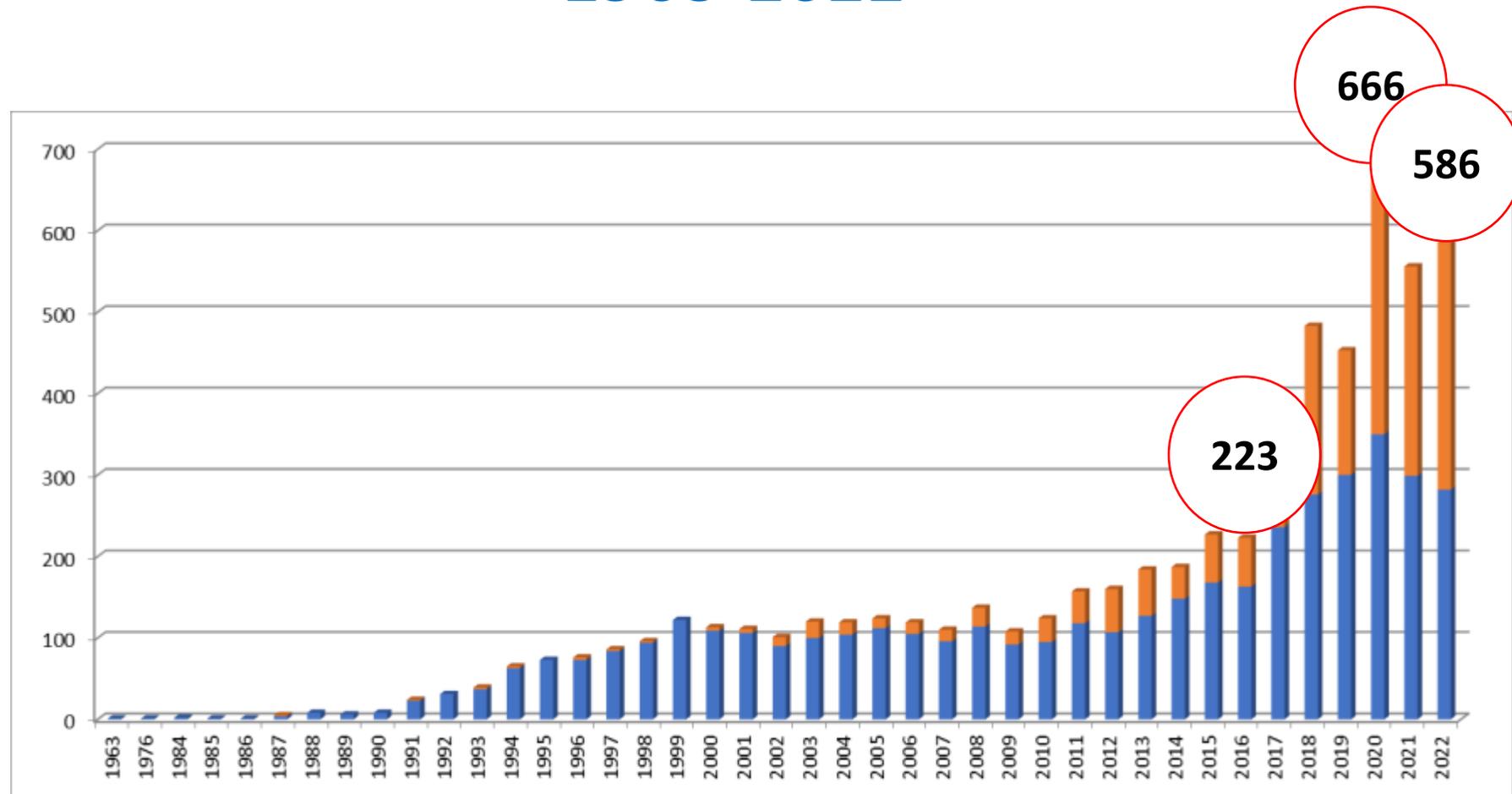
PDUFA VII Commitments

- CMC expectations have not changed
- CDRP Program
 - ✓ Requirements to participate in CDRP
 - ✓ How to apply to participate in CDRP
 - ✓ CDRP selection process

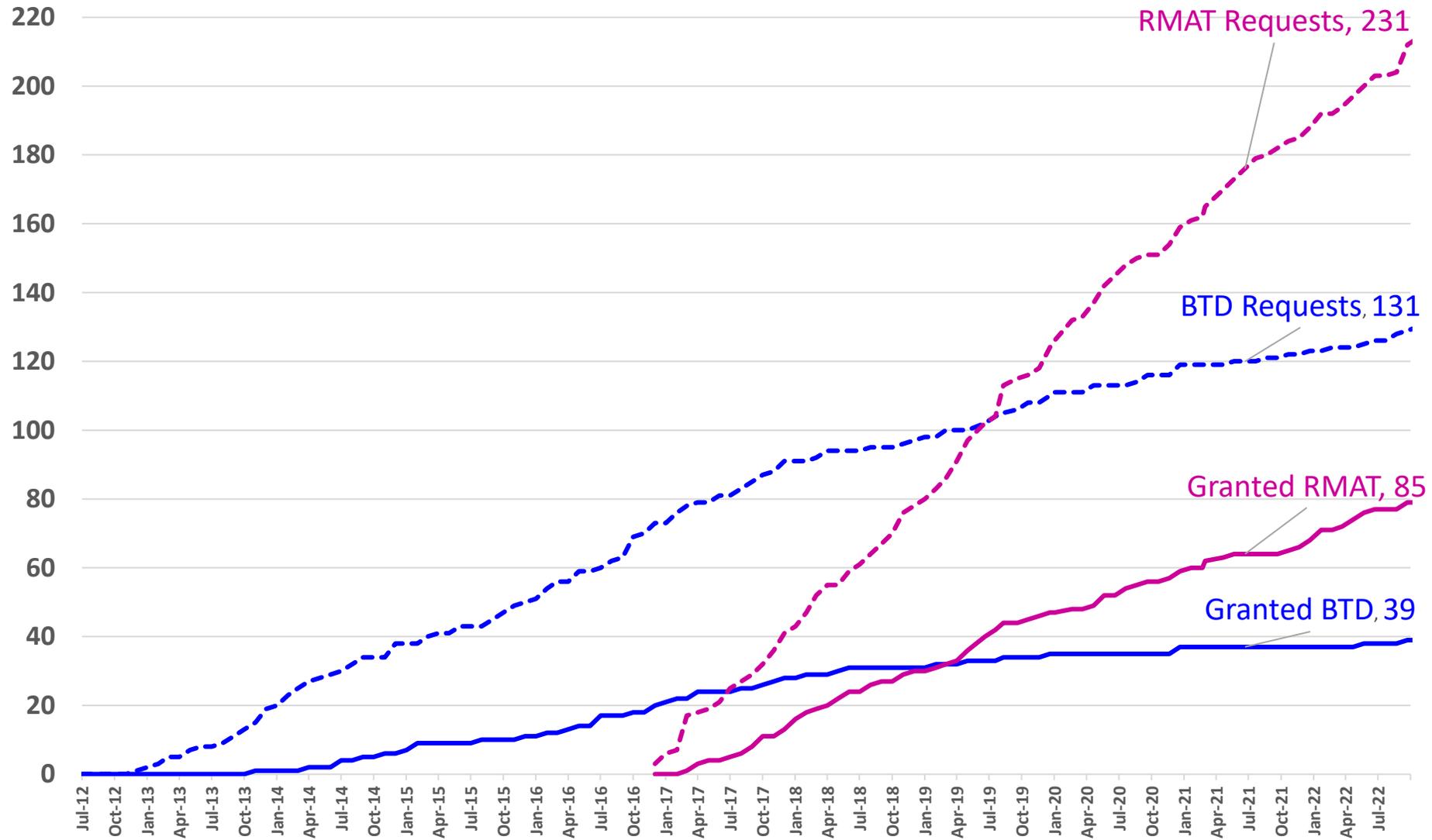
Summary

- Program is intended to help facilitate expedited CMC development of products through increased communication with FDA

OTP Research and Expanded Access (EA) INDs 1963-2022



Breakthrough (BT) and RMAT Designation Requests



Accelerated Clinical Development

- Innovative trial designs
 - Efficient clinical trial design strategies
 - Master clinical protocols: Basket trials
 - Possibility of a Phase II study to support licensure
- Possibility of product approval through surrogate endpoints
- Reduced clinical development timelines

However:

- ✓ No Changes to safety and efficacy standards
- ✓ **No changes to CMC requirements**

CDRP Program: The Need

CMC development often lags behind clinical progress in expedited programs

Sponsors need to prioritize CMC development early to prevent delays in product approval – Commitment to product development

Sponsors with expedited programs could benefit from additional interactions with FDA during product development, to help CMC keep pace with clinical development.



CDRP: Early Interactions with FDA Could Help Resolve CMC Related Development Issues

- CMC Development challenges Cell and Gene Therapy Examples
 - ✓ Development issues for a specific type of **vector manufacturing technology**
 - ✓ Development issues related to **purification/characterization/Lot release**
 - ✓ **Bioinformatics**, reference standards, levels of data gathered vs. required and issues with specific platforms based on sponsor's experience
 - ✓ Derivation of **personalized medicine products** and related issues
 - ✓ **Stability studies** (stability study design and issues face in completing stability)
 - ✓ **Assay validations** (types of assays and issues with validation studies and reference standards for the assays)

CDRP-Federal Register Notice (FRN)

DEPARTMENT OF HEALTH AND
HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2022-N-2396]

**Chemistry, Manufacturing, and
Controls Development and Readiness
Pilot Program; Program
Announcement**

AGENCY: Food and Drug Administration,
HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the opportunity for a limited number of applicants to participate in a Chemistry, Manufacturing, and Controls (CMC) Development and Readiness Pilot (CDRP) program, to facilitate the expedited CMC development of products under an investigational new drug (IND) application, where warranted, based upon the anticipated clinical benefit of earlier patient access to the products. FDA is implementing this pilot program to facilitate CMC readiness for selected Center for Biologics Evaluation and Research (CBER)- and Center for Drug Evaluation and Research (CDER)-regulated products with accelerated clinical development timelines. To accelerate CMC development and facilitate CMC readiness, the pilot features increased communication between FDA and sponsors and explores the use of science- and risk-based regulatory approaches, such as those described in FDA guidance, as applicable. This notice outlines the eligibility criteria and process for submitting a request to participate in the pilot.

CDRP Start Date : April 1, 2023

Duration of CDRP: 2023-2027 (PDUFA VII Period)

Sponsors of INDs with accelerated clinical development timelines are invited to apply to the CDRP

CDRP aims to:

- Encourage and facilitate the expedited CMC development of products
- Increase communication between FDA and sponsors
- Provide patients with earlier access to these products
- A total of 9 INDs will be selected each year (6 CBER and 3 CDER)

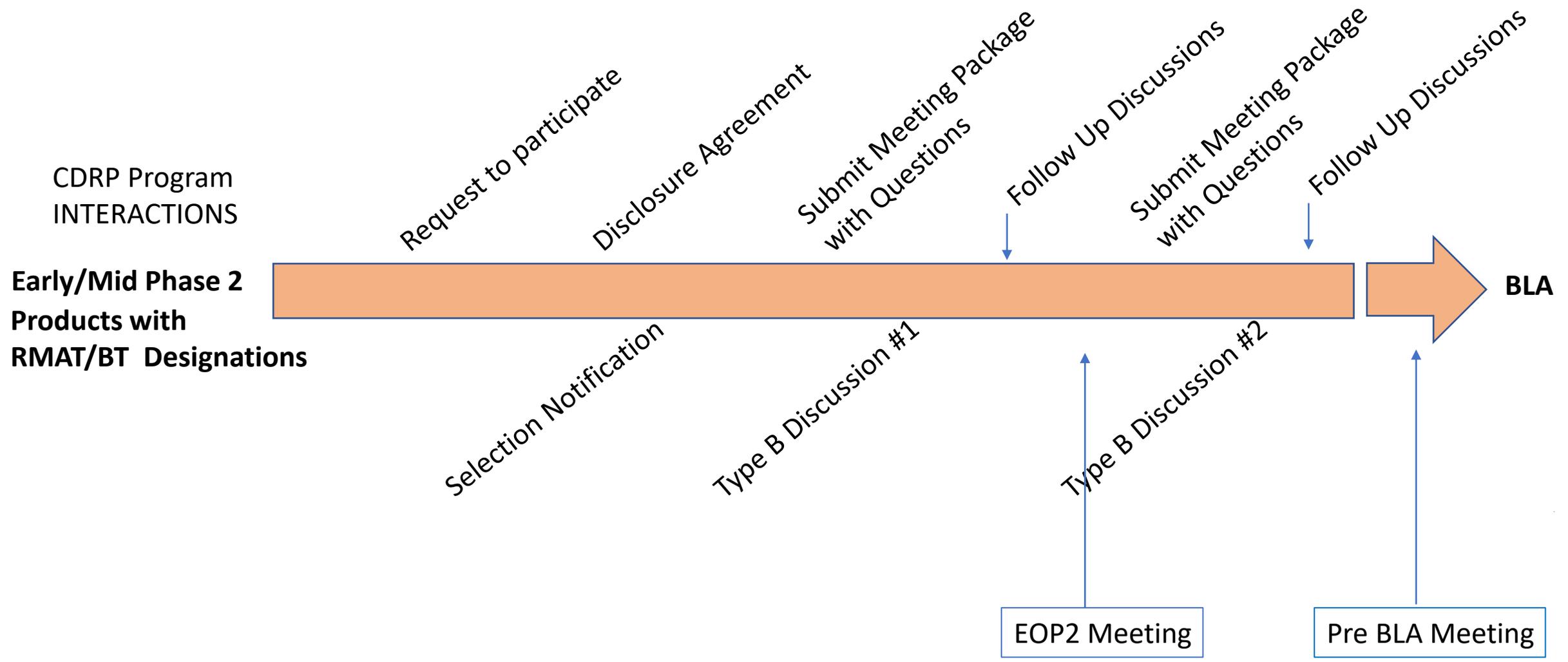
[Chemistry, Manufacturing, and Controls Development and Readiness Pilot \(CDRP\) Program | FDA](#)

CMC Development Readiness Pilot



- To Encourage sponsors to **take the initiative for product development earlier** in their clinical development program
- **Two dedicated CMC meetings** (Type B meetings, in addition to existing meetings)
 - Product specific guidance
- **Follow-up discussions** (To address questions arising from the meeting or meeting minutes)
- To **promote innovation** and understanding in this area, lessons learned through the pilot may be presented by FDA (*e.g.*, in a public workshop) as case studies.
- FDA intends to **issue a strategy** document focused on CMC aspects of expedited development incorporating lessons from the CDRP.

Schematic of CDRP Process Flow



CDRP Eligibility Criteria

Joint CBER and CDER Eligibility Criteria:

- IND is an active commercial IND
- IND has been submitted in, or converted to eCTD format, unless the IND is of a type granted a waiver from eCTD format
- IND should be before the end of Phase 2 (*exceptions allowed**)
- **Commitment to pursue CMC development plan that aligns with the expedited clinical development program**
- Combination products (21 CFR 3.2 (e)(1)) are eligible (*products that require significant cross-Center interactions (e.g., complex combination products) may be less likely to be selected for the pilot*)

FDA Center-Specific Eligibility Criteria (CBER)

CBER-Specific Eligibility Criteria:

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

FDA Center-Specific Eligibility Criteria (CDER)

CDER-Specific Eligibility Criteria:

- **An existing CDER-regulated IND** for a product intended for submission as an application for
 - ✓ Approval of a new drug submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)) (NDA)
 - ✓ Licensure of a biological product under section 351(a) of the PHS Act (BLA)
- **Products with expedited clinical timeframe**
 - ✓ A Breakthrough Therapy (BT), or Fast Track (FT) designation,
 - ✓ Other products that meet the BT/FT criterion may also apply to the Pilot, with their eligibility to be determined by FDA.

*Exceptions to “Prior to End of Phase 2” Requirements (Extenuating Circumstances)

FDA will assess the potential for benefit for a specific IND (*Product development programs expected to benefit from the pilot*)

Examples:

- Cases where the clinical development is following an innovative trial design (e.g., Complex Innovative Trial Design Program (CID*) participants eligible)
- The product is intended to treat a rare disease

* CID Program is for clinical trial design related discussions and places emphasis on products in late-stage drug development; and are not first-in-human trials.

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

- Submit a written request to participate to appropriate Center
 - Submit as an Amendment to the IND
- Include IND number and any expedited program designations received
 - ✓ BT (Date granted)
 - ✓ RMAT (Date granted)
- If you have any other active INDs provide a summary of the status of these INDs

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

- If you have other approved products, describe these products, and provide reference numbers
 - ✓ Include information on any approved products in foreign markets
 - ✓ Describe your level of manufacturing experience (similar product or different product type)
 - ✓ If you plan to use a CMO, provide a brief description of their manufacturing experience
- **Describe your CMC Development Plan***
- Is the IND on Hold for CMC reasons? If so please describe the status of the hold.
- Proposed plan and timing for meetings with FDA (as well as any other meetings and discussions foreseen)

CMC Development Plan

Describe your plans and preparation for commercializing your product:

- ✓ Current state of CMC development, including any ongoing activities not already included in the IND (proposed developmental plans e.g., new CMO/CTO plans, plans to move to new facilities)
- ✓ Available product characterization and preliminary identification of critical quality attributes (CQAs)
- ✓ Description of the current DS/DP **manufacturing process and control strategy** (including identification and development of assays) and a description of and **plan for the proposed commercial scale manufacturing** and control strategy, including any necessary microbial control strategy
- ✓ How you intend to establish a complete **supply chain for reagents**
- ✓ Overall **plan for process validation**
- ✓ Given the **expedited clinical timeframe**, mapping out a **plan for manufacturing readiness**, **highlight potential areas of challenge**

Test Question - 1

Who can apply to participate in CDRP?

- Sponsors who have an active IND
- Sponsors who have an IND in an eCTD format
- Sponsors who have a IND for a product with accelerated clinical development timelines

CDRP Selection Criteria

Review of requests will occur on a rolling basis and the sponsors will be informed of their application status within 180 days of the application.

FDA intends to consider:

- a) Anticipated clinical benefits of facilitating earlier patient access to the product
- b) Novelty of the product
- c) Complexity of the product or its manufacturing process (including technology)
- d) Sponsor's overall manufacturing experience*

*Sponsor's experience with the particular product type, class, or the type of manufacturing process (*less experienced manufacturer may be given additional consideration*).

Disclosure Agreement on Information That May Be Shared

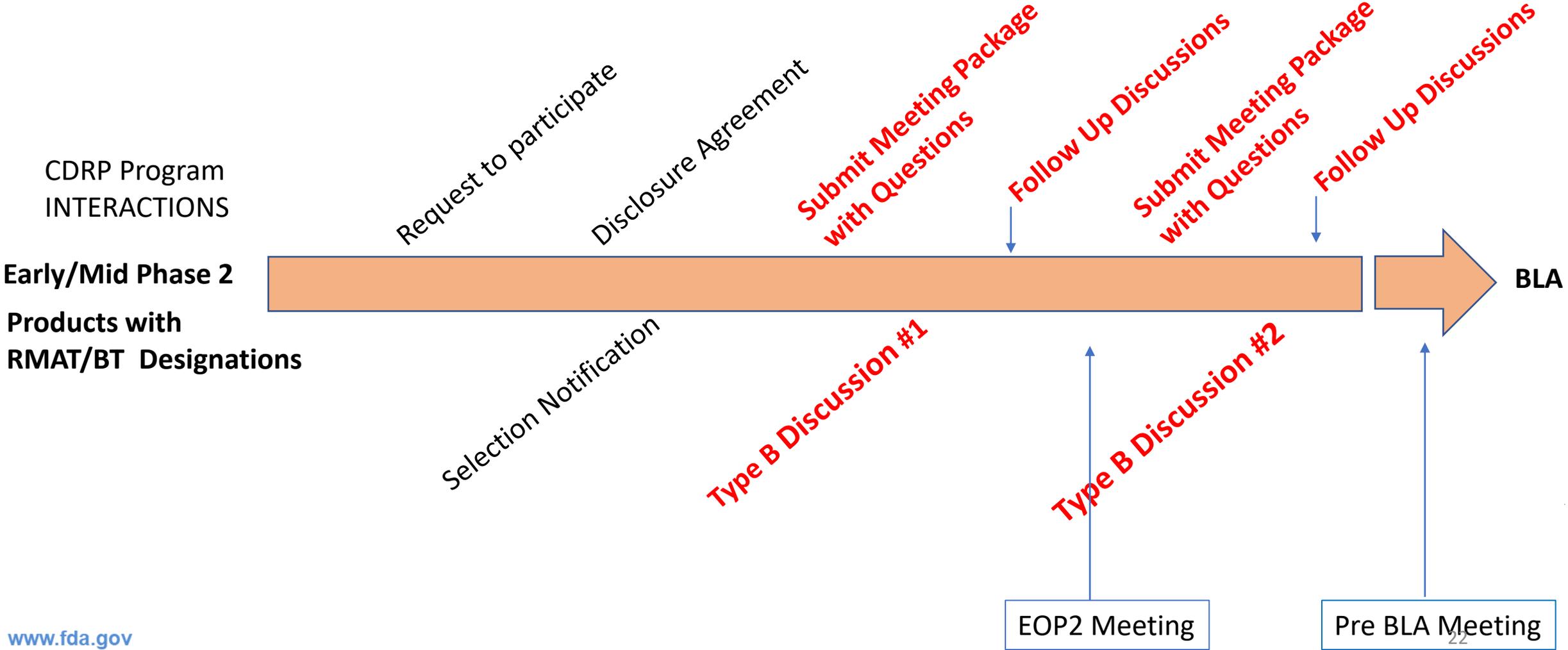
- To promote innovation and understanding in this area, lessons learned through the pilot may be presented by FDA (*e.g.*, in a public workshop) as case studies
- Shared information may include generalized case studies based on products in the pilot
- Information to be shared will be discussed and agreed between the sponsor and FDA
- A disclosure agreement letter template will be sent to the sponsors prior to final selection in the CDRP
 - ✓ **The disclosure agreement template will include examples of the type of information that will be disclosed**
 - ✓ **The disclosure agreement will be designed to share generalized information to help initiate discussions during the workshop**
- FDA will continue to ensure confidentiality of submitted information
 - ✓ **Not disclose information that is not agreed upon**

CBER CDRP Pilot Communications

- General Inquiries, CBER POC: Industry Biologics (industry.biologics@fda.hhs.gov)
- IND related communications: Assigned OTP Regulatory Project Manager
- Once the IND is accepted into the CDRP Program:
 - Submit a meeting request as an amendment to the IND
 - The Meeting request should include
 - ✓ A reference to the CDRP Program
 - ✓ A set of specific CMC questions
 - ✓ A meeting background package that explains/provides background information pertaining to the questions *

* Highly recommend the inclusion of a complete meeting package and questions with the meeting request

Schematic of CDRP Process Flow



Type B Meetings Under CDRP



- FDA will follow Type B meeting timeline (will be scheduled within 60 days of the request- per PDUFA, CBER SOPP 8101.1)
- In the meeting request
 - ✓ Submit questions
 - ✓ Highly recommend submitting a meeting package with the meeting request
- Sponsors can request the meeting format
 - ✓ Written response
 - ✓ Teleconference

Type B Meetings Under CDRP

- **FDA may change a requested response format**
- **If a teleconference format is granted**
 - ✓ FDA will provide a preliminary written response to the questions 2 days prior to the meeting (per PDUFA, CBER SOPP 8101.1)
 - ✓ Meeting minutes will be issued no later than 30 calendar days following the meeting (per PDUFA, CBER SOPP 8101.1)

Follow up Discussions

- Follow up discussions* may be in the form of
 - Teleconference
 - Written response
- Sponsors should send a written request with Questions as an amendment to the IND
 - The cover letter should mention CDRP in the subject line
 - Background related to the questions should be included with the request (if a direct follow up from FDA responses or clarification questions, the sponsor should reference the FDA communication)
 - Follow-up discussion will be scheduled per Type D meeting time lines (within 50 days)

* Follow up discussions are for questions arising out of the Type B meetings
Follow up discussions may be denied, if deemed inappropriate by FDA

Test Question - 2

What benefits can a CDRP participant expect to get from the program?

- Unlimited number of meetings with FDA review teams
- Advice on clinical trial design
- Two CMC focused meetings with FDA review team with a limited number of follow-up discussions

Workshop and Strategy Document

FDA intends to conduct a public workshop towards the later part of PDUFA VII period

- ✓ To promote innovation and understanding in CMC readiness of products under expedited clinical development
- ✓ Lessons learned through the pilot may be presented by FDA (*e.g.*, in a public workshop) as case studies
- ✓ Sponsors of INDs will also be asked to present their CDRP experience and lessons learned
- ✓ Lessons learned may also include those from CMC development of products that have not yet been approved by FDA
- ✓ FDA intends to follow-up with a strategy document focused on lessons from the CDRP

Summary

- The CMC Development Readiness Pilot (CDRP) is an FDA initiative to assist in CMC readiness of products under expedited clinical development
- CDRP's aim is to help sponsors meet the product safety and consistency standards for novel products designed to mitigate or treat serious and life threatening diseases or conditions
- Increase communication between FDA and sponsors
- CDRP started on April 1, 2023 and will continue till 2027 (PDUFA VII Period)
- A total of 9 Applications will be accepted per year during the pilot- 6 CBER and 3 CDER
- Sponsors of INDs with accelerated clinical development timelines are invited to apply to the CDRP
- The goal of CDRP is to provide patients with earlier access to new drugs and biologics

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- CBER website: www.fda.gov/BiologicsBloodVaccines/default.htm
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