PDUFA VII Enhancements

Interactions with OTP

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REdI – June 8-9, 2023

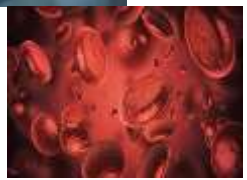
Learning Objectives

- Describe the new PDUFA VII opportunities for interactions with the Office of Therapeutic Products (OTP)
- Define INTERACT and Type D meeting requests and Requests for Clarification
- Describe the procedures and timelines associated with the meetings and requests

Diversity of Products Regulated by Office of Therapeutic Products in CBER

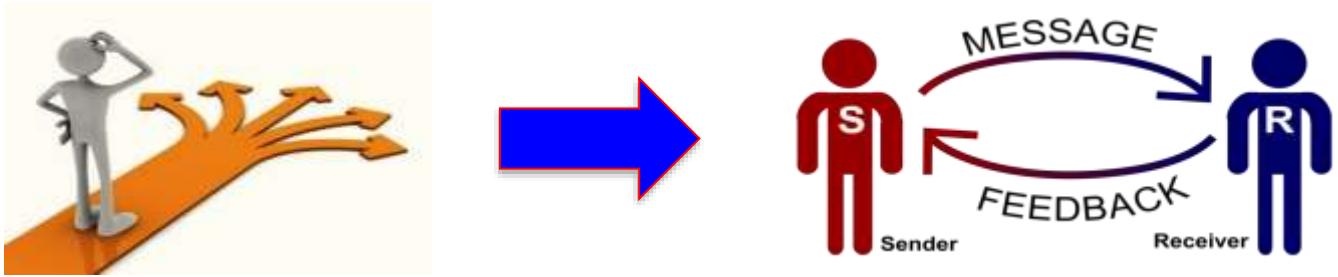
- **Gene therapies (GT)**
  - Ex-vivo genetically modified cells
  - Non-viral vectors (e.g., plasmids)
  - Replication-deficient viral vectors (e.g., adenovirus, adeno-associated virus, lentivirus)
  - Replication-competent viral vectors (e.g., measles, vaccinia)
  - Microbial vectors (e.g., Listeria, Salmonella)
  - Genome-edited products
- **Stem cells/stem cell-derived**
  - Adult (e.g., hematopoietic, neural, cardiac, adipose, mesenchymal)
  - Perinatal (e.g., placental, umbilical cord blood)
  - Fetal (e.g., neural)
  - Induced pluripotent stem cells (iPSCs)

- **Products for xenotransplantation**
- **Functionally mature/differentiated cells** (e.g., retinal pigment epithelial cells, pancreatic islets, chondrocytes, keratinocytes)
- **Therapeutic vaccines and other antigen-specific immunotherapies**
- **Blood- and Plasma-derived products**
  - Coagulation factors, fibrinogen, thrombin
  - Fibrin sealants
  - Plasminogen
  - Immune globulins
  - Anti-toxins
  - Snake venom antisera
- **Combination products**
  - Engineered tissues/organs
- **Devices**
- **Tissue-based products**



INTERACTIONS with OTP

- INTERACT Meetings- PDUFA
- Type D Meetings- New PDUFA meeting
- Request for Clarification



Important Info: [Update on In-Person Face-to-Face Formal Meetings with FDA]

INitial **T**argeted **E**ngagement for **R**egulatory **A**dvice on **C**BER/**C**DER Produc**T**s

(INTERACT) Meetings

What is an INTERACT Meeting?

- Formal meeting under PDUFA
- For novel therapies
- Allows sponsors to obtain early feedback
- Initial targeted discussion of specific issues

INTERACT Timing

- Investigational product identified
- Preliminary proof-of-concept studies conducted
- Definitive toxicology studies not yet designed and conducted
- **One** INTERACT meeting

INTERACT Discussions

- **CMC**
  - Issues and testing strategies aimed at demonstrating product safety to support first in human (FIH) clinical trials
- **Pharmacology/Toxicology**
  - Design of proof-of-concept or other pilot studies to support use in FIH clinical trials
- **Clinical**
  - Recommendations for FIH clinical trials in clinical population

INTERACT Request Process

- Official submission to CBER Document Control Center: cberdcc_emailsub@fda.hhs.gov or electronically via eCTD
- No acknowledgement of receipt from OTP
- Refer to CBER SOPP 8101.1: Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products

INTERACT Request Process

- ✓ Meeting package must accompany request
- ✓ Concise meeting package
- ✓ Key issues clearly identified

Meeting Package Best Practices

➢ Chemistry, Manufacturing, and Controls (CMC)

- Summary of product, manufacturing process, proposed characterization, lot release tests
- Sponsor's position and justification for questions
- References to published information

Chemistry, Manufacturing, and Control (CMC) Information for Human Gene Therapy Investigational New Drug Applications (INDs)

Guidance for FDA Reviewers and Sponsors: Content and Review of Chemistry, Manufacturing, and Control (CMC) Information for Human Somatic Cell Therapy Investigational New Drug Applications (INDs)

Meeting Package Best Practices

- **Pharmacology/Toxicology**
  - Comprehensive summary of preclinical studies
  - Detailed discussion of additional proof-of-concept studies
  - Sponsor's position and justification for questions
- Do not include questions regarding definitive preclinical safety studies

Guidance for Industry: Preclinical Assessment of Investigational Cellular and Gene Therapy Products

Meeting Package Best Practices

➢ Clinical

- Disease of interest
- Target study population
- Available natural history information/data on condition
- Available treatment options
- Brief outline of first-in-human study

INTERACT Request Review

- Grant or deny decision within 21 days
- Request and package must be complete
- Written Response Only (WRO), teleconference, or face-to-face
- Meeting confirmation via email

INTERACT Meeting or WRO Timeline

- Meeting scheduled within 75 calendar days
- WRO goal date by Day 75
- Preliminary Responses sent 5 days prior to meeting date
- Sponsor response within 3 days of receipt
- No formal meeting minutes
- Annotated preliminary responses within 30 days if advice changed

INTERACT Meeting Denial

- No meeting package or deficient package
- A meeting was previously held
- Requested feedback not appropriate
- Stage of development premature or too advanced

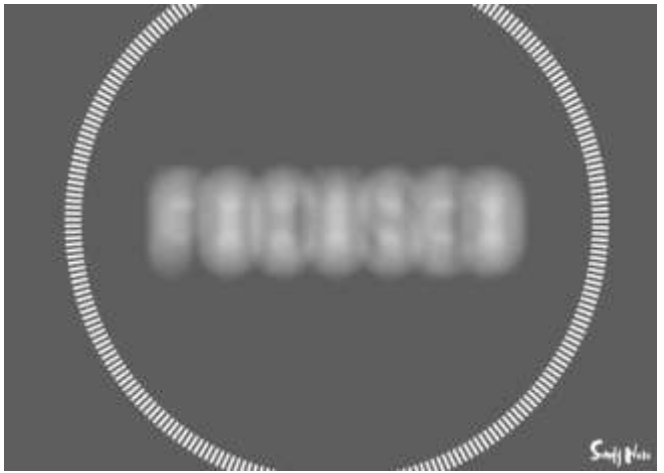
Premature for INTERACT

- Investigational Product not specified
- Preclinical proof-of-concept (POC) or pilot data not provided
- No preclinical studies with intended product have been conducted

Too Advanced for INTERACT

- If too advanced, **may be** converted to Pre-IND
  - Completed proof-of-concept (POC) and some safety studies; at point of design and conduct of definitive tox studies
  - Defined manufacturing process; developed assays and preliminary lot release criteria
  - Pre-clinical testing and manufacturing process uses same/similar platform
  - Clinical data exist

Type D Meetings



What is a Type D Meeting?

- New PDUFA meeting type
- Focused on narrow set of issues
- Questions do not require input from more than 3 disciplines
- Discuss issues at key decision points
- Timely feedback is critical to move program forward

Type D Timing and Considerations

- Requested at any point in development program
- Consider needs before request
- INTERACT and Pre-IND should be able to address critical IND enabling issues

Type D Considerations

- Consider number and complexity of issues
- If several issues, request Type C or Type B
- Avoid multiple Type D meeting requests
- Type C for complex single issue with multiple questions

Type D Request Process

- ✓ Official submission
- ✓ Meeting package must accompany request
- ✓ Grant or deny decision within 14 days
- ✓ WRO, teleconference, or face to face
- ✓ Meeting confirmation via email

Type D Meeting or WRO Timeline

- Meeting scheduled within 50 days
- WRO goal date by Day 50

- Preliminary Responses sent 5 days prior to meeting date
- Sponsor responses within 3 day of receipt
- Formal meeting minutes within 30 days

Meeting Conversion

- **May** convert to Type B or Type C
- Resubmission not required
- Meeting package can be revised
- Sponsor can withdraw request

Meeting Denial

- No meeting package
- Topic and questions too broad
- Previous meeting for same purpose held
- Requested feedback not appropriate

Appropriate Type D Requests

- A follow-up question that raises a new issue after a formal meeting.
- A narrow issue on which the sponsor is seeking OTP input with only a few associated questions.
- A general question about an innovative development approach that does not require extensive, detailed advice.

Examples of Type D Meetings in OTP

- Specific question about a proposed potency assay method before validation study
- Requesting advice on strategy and stability data requirements for shelf-life extension
- Feedback on updated study data plan
- Post Type C meeting advice on interim analysis

Meeting Summary

Meeting Type	Grant or Deny	Meeting Package	Preliminary Response Sent	Response from Sponsor	Meeting Date or WRO	Meeting Minutes
INTERACT	21 Days	With Request	5 days before meeting	Within 3 days of receipt of preliminary comments	Within 75 Days	Annotated Preliminary Responses – 30 days after meeting, if applicable
Type D	14 Days	With Request	5 days before meeting	Within 3 days of receipt of preliminary comments	Within 50 Days	30 Days after meeting

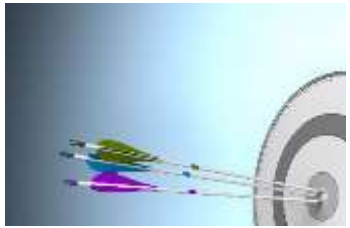
Requests for Clarification

Requests for Clarification

- Formalized process
- Clarification of meeting discussion and written responses
- Applies to all PDUFA meeting types
- Applies to all final meeting document types

Scope of Requests

- Only questions of clarifying nature
  - Confirm a statement by OTP



- Not raising new issues or new proposals
- No new data, protocols, or information needed to respond

Request Process

- Submitted as amendment to original meeting
- Received within 20 days of issuance of final meeting document
- OTP determines if in-scope
- OTP responds via email within 20 days

Out of Scope

- Treated as general correspondence
- No review timeline
- Respond as resources allow

Out of Scope Examples

- Questions related to new information not included in the briefing package
- Questions related to the adequacy of new proposals to address OTP comments

Request for Clarification Summary

Meeting Type	Clarification of Meeting Document	Request Receipt Date	Request Response Date	Response Type
All PDUFA Meetings	Written Response (WRO), Preliminary Response if no meeting, Meeting Minutes	Within 20 days of issuance of Meeting Document	20 days after receipt of request	Written via email

Challenge Questions

Challenge Question #1

Which of the following statements is NOT true?

A. Formal meeting minutes for INTERACT meetings are sent within 30 days of the meeting.

B. OTP will respond to requests for clarification within 20 days of receipt.

C. INTERACT meetings are scheduled by Day 75.

D. Type D meetings are narrow focused meetings.

Challenge Question #1

Which of the following statements is NOT true?

A. Formal meeting minutes for INTERACT meetings are sent within 30 days of the meeting.

B. OTP will respond to requests for clarification within 20 days of receipt.

C. INTERACT meetings are scheduled by Day 75.

D. Type D meetings are narrow focused meetings.

Challenge Question #2

Requests for clarification should be received within how many days from issuance of the final meeting document:

A. 15 days

B. 75 days

C. 20 days

D. 60 days

Challenge Question #2

Requests for clarification should be received within how many days from issuance of the final meeting document:

A. 15 days

B. 75 days

C. 20 days

D. 60 days

Challenge Question #3

Which of the following statements is true?

A. INTERACT meetings are granted within 14 days

B. Meeting packages must be submitted with an INTERACT or Type D Meeting Request

C. Requests for clarification are related to new INDs

D. Type D meetings are scheduled within 75 days

Challenge Question #3

Which of the following statements is true?

A. INTERACT meetings are granted within 14 days

B. Meeting packages must be submitted with an INTERACT or Type D Meeting Request

C. Requests for clarification are related to new INDs

D. Type D meetings are scheduled within 75 days

Resources

- Interactions with Office of Therapeutic Products
- CBER SOPP 8101.1: Regulatory Meetings with Sponsors and Applicants for Drugs and Biological Products
- CBER JA-820.13: Procedure for Requests for Clarification

Resources

- Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products
- Best Practices for Communication Between IND Sponsors and FDA During Drug Development
- Update on In-Person Face-to-Face Formal Meetings with FDA

Resources

- Prescription Drug User Fee Amendments
- OTP Learn- Webpage for Industry Education

Summary

- There are three new ways to interact with OTP
- INTERACT meetings are formal PDUFA meetings
- Type D meeting is a new meeting type for narrow focused issues
- Requests for clarification are available for all meeting types and formats

OTP looks forward to future collaboration.

Contact Information

- **Mara Miller: mara.miller@fda.hhs.gov**
- **Regulatory Questions:**
  OTP Main Line – 240 402 8190
  Email: OTPRPMS@fda.hhs.gov

- **Interactions with Office of Therapeutic Products website:**
  Interactions with Office of Therapeutic Products | FDA

- **OTP 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.hhs.gov

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Questions?

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