Guidance for Industry: Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products

Jeannie Roule
Chief, Project Management Staff
Division of Regulatory Operations for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Office of Regulatory Operations
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration

Meetings with the FDA

Why, When, and How

Agenda

- Types of meetings and their timelines
- Milestone meetings and their objectives
- How to request a meeting
- Meeting granted-What to expect
- Comments and Best Practices
- Biosimilar User Fee Act (BsUFA)

Discussion between FDA and Sponsor

- Sponsors and FDA work collaboratively during the drug development process, having a shared public health goal of early availability of safe, effective, and high-quality drugs to the American public.
- Sponsors can seek answers to their scientific and regulatory questions from the multitude of resources available to them
- Independent consultants?
- Discuss with FDA complex and challenging drug development and regulatory science issues.

Why are Meetings Important?

- Meetings between FDA and a sponsor at critical junctures in drug development can be especially helpful in minimizing wasteful expenditures of time and resources, thus speeding the drug development and evaluation process.
- Meetings are useful in resolving questions and issues raised during development programs.
- FDA can provide valuable scientific and regulatory advice, resulting in more efficient and robust development programs.

What Types and Format of PDUFA Meetings are Available?

- Several different types of meetings:
  - Type A, Type B, and Type C
- Formats:
  - Teleconference/videoconference
  - Written Responses Only (WRO)
  - Face-to-Face*

*current pause for face-to-face

Meeting Type	Respond Within:	Meeting Scheduled WRO Due Within:	Background Package Due:	Preliminary Comments Due:
A	14 days	30 days	At time of request	24-48 hours before meeting
B	21 days	60 days	30 days before meeting/WRO	24-48 hours before meeting
B(EOP)	14 days	70 days	50 days before meeting/WRO	**PDUFA VI: 5 days before meeting**
C	21 days	75 days	47 days before meeting/WRO	**PDUFA VI: 5 days before meeting**
C (new surrogate endpoints)	21 days	75 days	At time of request	24-48 hours before meeting

Type A Meeting

- **Stalled Development:**
  - Dispute resolution
  - Clinical Hold
  - Nonagreement to Special Protocol Assessment
  - Post-Action (must be requested within 3 months of the regulatory action, other than approval)
  - Post Refuse to File (must be requested within 30 days of FDA issuance of RTF letter)

Type B Meeting

- Pre-IND meeting
- Pre-NDA/BLA meeting
- Pre-EUA meetings
- Post-action meetings (if requested 3 months or more after complete response action)
- Meetings regarding REMS and Postmarketing Requirements
- Overall development program for products granted breakthrough therapy designation
- COVID 19 products

Type B End of Phase Meeting

- Certain End-of-phase 1 meetings
  - products that will be considered for marketing under 21 CFR part 312, subpart E
  - Products that will be considered for marketing under 21 CFR part 314, subpart H
  - Or similar products
- End-of-phase 2 meetings or pre-phase 3
- Carry slightly different regulatory timelines from other type B meetings

Type C Meeting

- Anything else
- For example:
  - Advice or guidance meetings
  - Early consultation on the use of biomarkers as a new surrogate endpoint not previously used as the primary basis for product approval in the proposed context of use

Pre-IND Meeting 21 CFR 312.82(a)

- Objectives:
  - Review and reach agreement on the design of animal studies needed to initiate human testing
  - Discuss the scope and design of Phase 1 testing
  - Plans for studying the drug product in pediatric populations
  - Approach for presentation and formatting of data in the IND

When and Why

- New Molecular Entity (NME)
- Novel indication
- No current Guidance Documents
- Unique molecular entity, studies or indication(s)

When and Why

- New sponsors or new to area of drug development
- Animal Rule development program
- Problematic Pharm/Tox signals
- Avoid protocol changes

Pre-IND Meeting

- Meeting can be addressed by “written response only” (WRO)
  - Requested by sponsor or Determined by FDA
- Response to questions by day 60 from the receipt date
- Meeting package at least 1 month in advance of the response goal date

Pre-IND Meeting Request

Pre-IND File

- No regulatory prerogatives
- No clinical study can be conducted
- No need for US Representative

An acknowledgment letter is sent to the sponsor

All future communications should refer to this PIND number

PIND number is converted to IND number after IND submission (file number carries over)

Pre-IND Meeting Briefing Document

- More detailed than the meeting request
- Provide summary of information relevant to the product and any supplemental information needed to address the questions
- Organized according to the agenda and questions
- Table of contents

End of Phase 1 Meeting (EOP1) 21 CFR 312.82

- Generally reserved for drugs for severely-debilitating and life-threatening illnesses reviewed under the accelerated approval program

- Objective:
  - Review and reach agreement on the design of Phase 2 controlled clinical trials
  - Discuss the need for, as well as design and timing of studies in pediatric patients

End of Phase 2 (EOP) Meeting 21 CFR 312.47 (b) (1)

- Objectives:
  - Obtain agreement on pivotal study designs, and safety and efficacy endpoints for Phase 3 studies
  - Update progress of PK studies and discuss additional studies needed
  - Assure pre-clinical data regarding duration, route of administration, and formulation are supportive of the dose to be used in clinical trials

EOP2 Meeting (cont.)

- Discuss approach to specifications and test methods
- Discuss “to be marketed” formulation
- Evaluate appropriate stability protocols
- Identify other issues or potential problems (novel regulatory or technical concerns)

EOP2 Meeting Briefing Package

- Summaries of Phase 1 and Phase 2 investigations
- Plans for pediatric studies
- Plans for additional non-clinical studies (if required)
- Summary information on plans for Phase 3 trials
- Specific protocols for Phase 3 studies

Pre-NDA/BLA Meeting

- Objectives:
  - Determine the adequacy of the sponsor's dossier for the submission of an NDA/BLA
  - Determine status of ongoing studies to address pediatric safety and efficacy
  - Early discussions on priority or standard review, and need for Advisory Committee meetings

Pre-NDA/BLA Meeting (cont.)

Objectives (cont):

- May include discussion on the need for REMS (Risk Evaluation and Mitigation Strategies) plans and proposed observational studies
- To agree on format and content of the application
    - All new applications must be submitted in eCTD format through the gateway (ESG)

Pre-NDA/BLA Briefing Document

- Summary of the data from completed pivotal studies
- Proposed indication
- Manufacturing information on the products used in the studies and product intended for distribution, if different.

Pre-NDA/BLA Briefing Document

- Discussion on request for priority review and Advisory Committee
- Information on Fast Track, Orphan Product status, Breakthrough Therapy designation if pertinent
- Pediatric Information
- Timeline for submission

Pre-NDA/BLA Meeting 21 CFR 312.47 (b) (2)

Critical interaction between FDA staff and the sponsor in ensuring the submission of a well organized and readily reviewable NDA/BLA

Feel confident it will be complete and accurate.

How to request a Pre-IND meeting

- Submission of a meeting request
  - New Pre-IND
    - NextGen portal
    - eCTD/ESG
    - Paper-Mail to FDA
    - Know your FDA Division, if possible
    - If you have questions, contact the CPMS

Submission Pathways

Type of Submission	Submission Pathway
PIND: Research or Commercial	NextGen eCTD/ESG Mail/Paper copy
Research IND	NextGen eCTD/ESG Mail/Paper copy
NDA	eCTD/ESG
BLA	eCTD/ESG
For an application number only:	NextGen Or send email to: cderappnumrequest@fda.hhs.gov

What happens after you submit your meeting package?

- For all Type A, B and C meetings, there is at least one internal team meeting
  - Team discusses and reaches agreement on responses
  - Preliminary responses to questions are sent to the sponsor as many as 5 days before the meeting and no later than 48 hours before the meeting (refer to table on slide 7)

Before the Meeting

- Review preliminary responses
- Alert RPM if FDA responses were sufficient and no formal meeting is necessary
- Meeting would then be cancelled, and the preliminary responses become the formal meeting minutes
- Alert RPM if clarification is needed on a specific question(s).

Before the Meeting (cont.)

- Provide an outline of the specific questions and include your any additional rationale
- Do not add new topics or issues to the original agenda
- Provide any meeting slides/revised proposal, if possible before the meeting
- Notify RPM of any changes to the list of attendees

During the Meeting

- Do not spend a lot of time on the presentation.
- The FDA is familiar with your program based on the information in your meeting package.
- Use the time for discussion
- Share your concerns, and propose solutions
- Stay focused on the agenda
- Be clear with your rationale
- Listen closely and strongly consider recommendations

During the Meeting (cont.)

THIS IS YOUR MEETING
Take the lead

- Make sure that your questions have been addressed
- You should summarize key discussion points, agreements, action items
- Any lingering questions or concerns, you need to come to an agreement with the FDA as to how they will be addressed.

Post Meeting

- Submit any meeting slides to the application
- Official FDA minutes will be issued within 30 days of the meeting
- Review minutes and notify Division of any discrepancies/clarifications
- Follow-up on any requests

Best Practices

- Establish a relationship and communicate clearly with the RPM
- Establish a secure email
- Know your Division
- All cover letters should clearly state your intentions
- All questions in a meeting request/package should be focused, and clear

Best Practices

- Limit the number of questions so they can be answered in the allotted timeframes
- Include adequate information to support intended objectives
- Organize the briefing package with TOC and hyperlinks
- Previously submitted data should be noted and include the original submission date

Best Practices

- Follow the same grammatical, punctuation, numbering, abbreviation, and document conventions and maintain the integrity of the document formatting and styles.
- Review for inconsistencies
- Meeting package-DO NOT BE LATE
- Use your time wisely

Biosimilar User Fee Act (BsUFA) Meetings

- Biosimilar Initial Advisory Meeting
- Biosimilar Product Development Type 1
- Biosimilar Product Development Type 2
- Biosimilar Product Development Type 3
- Biosimilar Product Development Type 4
- Non PDUFA Meeting

Biosimilar Initial Advisory Meeting

- No fee
- Response goal date within 21 days of FDA receipt of a meeting request with briefing document
- Held within 90 calendar days of FDA receipt of meeting request
- Minutes issued within 30 days of the meeting

Biosimilar Product Development Type 1

- Necessary for an otherwise stalled biosimilar development program
- FDA will not hold the meeting unless the yearly fee has been paid
- Meeting response within 14 days of FDA receipt of a written meeting request and meeting package
- Held within 30 days of the meeting request
- Minutes issued within 30 days of the meeting

Biosimilar Product Development Type 2

- Targeted advice regarding a discrete issue
- May include review of data but not review of full study reports
- FDA will not hold the meeting unless the yearly fee has been paid
- Meeting response within 21 days of FDA receipt of a written meeting request and meeting package
- Held within 75 days of the meeting request
- Minutes issued within 30 days of the meeting

Biosimilar Product Development Type 3

- In depth review of study reports
- FDA will not hold the meeting unless the yearly fee has been paid
- Meeting response within 21 days of FDA receipt of a written meeting request and meeting package
- Held within 120 days of the meeting request
- Minutes issued within 30 days of the meeting

Biosimilar Product Development Type 4

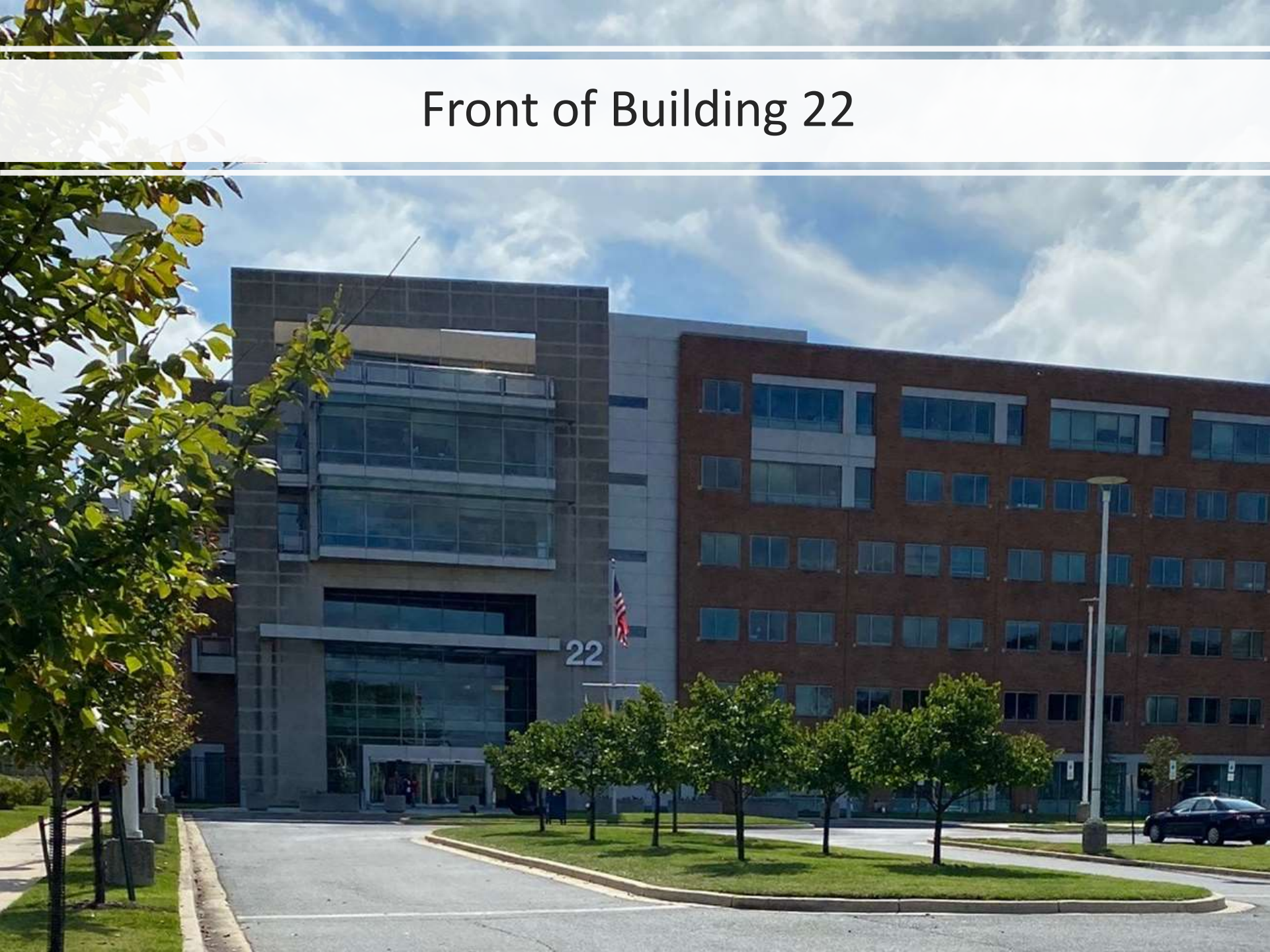
- Discussion of format and content of a biosimilar product application
- FDA will not hold the meeting unless the yearly fee has been paid
- Meeting response within 21 days of FDA receipt of a written meeting request and meeting package
- Held within 60 days of the meeting request
- Minutes issued within 30 days of the meeting

Meeting Location

Food and Drug Administration
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Silver Spring, MD 20993

Entrance to FDA in White Oak

Front of Building 22



Anchor in front of Building 22

- The current site of the FDA, used to be a remote area with only farmlands.
- Around 1944 until 1995, the Naval Ordnance Laboratory research facility was in this location.
- 1995, the site was transferred to the General Services Administration.
- 1996, the site was renamed the Federal Research Center at White Oak

Resources

Main FDA Website:
www.fda.gov
- www.fda.gov/Drugs
- www.fda.gov/BiologicsBloodVaccines
- www.fda.gov/MedicalDevices

Best Practices for Communication Between IND Sponsors and FDA During Drug Development:
Best Practices for Communication Between IND Sponsors and FDA During Drug Development | FDA

Biosimilar User Fee Amendments
www.fda.gov/bsufa

Biosimilar User Fee: Additional Information
Assessing User Fees Under the Biosimilar User Fee Amendments of 2017 Guidance for Industry | FDA

Biosimilar and Interchangeable Products:
https://www.fda.gov/drugs/biosimilars/biosimilar-and-interchangeable-products

Resources

Chief, Project Management Staff (for Office/Division):
Office of Regulatory Operations (sharepoint.com)

COVID 19 Meetings:
https://www.fda.gov/media/137927/download

Electronic Common Technical Document (eCTD)
https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd

FDA Guidance Documents by Topic:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents

Formal PDUFA Products Meetings Guidance:
https://www.fda.gov/media/109951/download

Resources

Formal BsUFA Products Meetings:
https://www.fda.gov/media/113913/download

How Drugs are Developed and Approved (Application types and other resources):
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved

NextGen Portal
https://edm.fda.gov/

NextGen Portal more Information
https://www.fda.gov/drugs/news-events-human-drugs/still-submitting-paper-cder-send-electronically-cders-nextgen-portal-instead-submissions-not

Resources

Office of New Drugs: Office Organization
https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/office-new-drugs

Pre-Assigned Application number: How to Request
https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/requesting-pre-assigned-application-number

Prescription Drug User Fee Act Reauthorization (PDUFA VI)
https://www.fda.gov/news-events/congressional-testimony/prescription-drug-user-fee-act-reauthorization-pdufa-vi-medical-device-user-fee-act-reauthorization

Resources

Secure Email:
SecureEmail@fda.hhs.gov

Surrogate Endpoints:
https://www.fda.gov/drugs/development-resources/surrogate-endpoint-resources-drug-and-biologic-development

User Fees Under the Prescription Drug User Fee Amendments
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/assessing-user-fees-under-prescription-drug-user-fee-amendments-2017-guidance-industry

Thank you for your time!