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# *Pre-Submission Considerations*

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# Learning Objectives

- Develop a  better understanding of processes, requirements, and best practices for PDUFA meetings.
- Develop an understanding of programs that may effect the review process or timelines for an application.

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# Formal PDUFA Meetings with FDA

# Request and Requirements

The meeting request **must** include the following information:

1. The proposed meeting format
2. The date the meeting background package will be sent by the requester
3. A brief statement of the purpose of the meeting.
4. A list of the specific objectives or outcomes.
5. A proposed agenda.
6. A list of planned attendees from the requester's organization.
7. A list of requested FDA attendees and/or discipline representative(s).

# Requests and Requirements

The meeting request **should** include the following information:

1. The application number.
2. The product name.
3. The chemical name, established name, and/or structure.
4. The proposed regulatory pathway
5. The proposed indication
6. The meeting type being requested.
7. Pediatric study plans
8. Human factors engineering plan
9. Combination product information
10. Suggested dates and times.
11. A list of proposed questions

# Meeting Granted

| Meeting Type (any format) | Response Time (calendar days from receipt of meeting request/WRO request) |
|---|---|
| A | 14 days |
| B | 21 days |
| B (EOP) | 14 days |
| C | 21 days |

# Meeting Denied

- Meeting request does not contain substantive required elements (see previous slides).
- Meeting is premature for the stage of product development.
- Generally, the FDA will not grant more than one of each of the Type B meetings.

# Meeting Package Timelines

| Meeting Type | FDA Receipt of Meeting Package (calendar days) |
|---|---|
| A, C* | At the time of the meeting request |
| B | No later than 30 days before the scheduled date of the meeting or WRO response time |
| B (EOP) | No later than 50 days before the scheduled date of the meeting or WRO response time |
| C | No later than 47 days before the scheduled date of the meeting or WRO response time |

# Meeting Package Contents

- The application number.
- The product name
- The chemical name, established name, and/or structure
- The proposed regulatory pathway
- The proposed indication(s) or context of product development.
- The dosage form, route of administration, and dosing regimen.
- Pediatric study plans, human factors engineering plan, and Combination product information, if applicable.

# Meeting Package Contents Continued

- A list of all attendees
- A background section
- A brief statement identifying the purpose of the meeting
- A proposed agenda
- A list of the final questions for discussion
- Data to support discussion

# Best Practices: Pre-NDA/BLA Meetings

- Submit no less than 2 month prior to planned submission
- Pre –Submission meetings familiarize FDA reviewers with the format and content of the planned marketing application

# Best Practices: Pre-NDA/BLA Meetings

- They are also intended to uncover major issues
- FDA encourages sponsors to request pre-NDA/BLA meetings for all planned marketing applications

# Communication Best Practices

- Develop a mutually agreeable communication strategy early in development
- A formal communication plan may be established for drug applications reviewed in the Program
- A formal communication plan should also be established for breakthrough therapy-designated drugs

# Communication Challenges

- Communication with next level supervisor
- Communication with review team supervisors or management officials

# OND Communications

- Responds to general questions about the drug review process
- Clarifies which OND review division to contact
- Provides assistance resolving communication challenges with the review team

ONDCommunications@fda.hhs.gov

# Ombudsman

Provides:

- informal advice or referrals
- assistance with issues that arise in the context of the regulatory process
- feedback about CDER's programs and overall performance

Note: Upon request, communication with the Ombudsman will be kept confidential.

CDER Ombudsman web page: https://www.fda.gov/about-fda/cder-contact-information/cder-ombudsman

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# Application Considerations

# Priority vs. Standard Review

- Standard Review
  - Non- NME/ Original BLA: 10 month clock
  - NME/Original BLA (products under the Program): 12 month clock
- Priority Review
  - Non- NME/ Original BLA: 6 month clock
  - NME/Original BLA (products under the Program): 8 month clock

# FDA Expedited Programs

- Goal of the 4 programs: To facilitate and expedite review of new drugs to address unmet medical need in the treatment of serious or life-threatening conditions

- Guidance to Industry: Expedited Programs for Serious Conditions-Drugs and Biologics, May 2014

# Priority Review

- Criteria:
- An application for a drug :
  - That treats a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness OR
  - That proposes a labeling change pursuant to a report on a pediatric study under 505A OR
  - That has been designated as a qualified infectious disease product OR
  - Submitted with a priority review voucher
- Features:
  - Shorter clock for review of marketing application compared with standard review

# Accelerated Approval

- Criteria:
- A drug that:
  - treats a serious condition AND ,
  - provides meaningful advantage over available therapies AND
  - demonstrates effect on surrogate endpoint
- Features:
  - Approval based on an effect on surrogate endpoint

**Accelerated Approval: Section 506(c) Food, Drug & Cosmetic Act (FD&C Act) of the FD&C Act of 1992, amended by section 901 of FDASIA**

# Fast Track

- Criteria:
  - A drug that:
    - Is intended to treat a serious condition AND nonclinical or clinical data demonstrate the potential to address unmet medical need OR
    - That has been designated as a qualified infectious disease product
- Features:
  - FDA takes actions to expedite development and review
  - Eligible for rolling review

**Fast Track: Section 506(b) of FD&C Act added by section 112 of the Food and Drug Administration Modernization Act of 1997 (FDAMA), amended by section 901 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)**

# Breakthrough Therapy

- Criteria
  - Serious condition
  - Preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on one or more clinically significant endpoints
- Features
  - Intensive guidance on efficient drug development
  - Organizational commitment
  - Eligible for rolling review

Breakthrough Therapy Designation: Section 506(a) of the FD&C Act, as added by section 902 of FDASIA, 2012

# The Program: Basics

- The Program started under PDUFA V for NME NDAs and original BLAs
- Focus on enhanced communication with applicant in order to achieve Program goals
- PDUFA clock includes 2 additional months to address activities that occur late in the review cycle

# Changes to the Program under PDUFA VI

- Formal Communication Plan
- Expedited reviews
- "Filed over Protest" applications
- Scheduling recommendations
- Application Orientation Meeting
- Mid-Cycle Communication
- Late-Cycle Meetings and Background Packages
- Advisory Committee Meetings
- Discipline Review Letters

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# Advisory Committee Meetings

https://www.fda.gov/advisory-committees/about-advisory-committees

# What Are Advisory Committees (AC)?

- Any committee, board, commission, council, conference, panel, task force, or similar group which is established and utilized by statute, President or any Agency in order to obtain advice or recommendations.
- Committees composed of full-time officers or employees of the federal government do not count as *advisory committees* under the Federal Advisory Committee Act (FACA).

# Why Hold an AC?

- Drug or biologic that is novel
- NDA/BLA raises an important safety issue
- NDA/BLA raises substantive issues in interpretation
- Product has broad public health implications
- There is a fundamental disagreement
- New endpoints

# Advisory Committee Makeup

**Voting Members**

- Chairperson
- Consumer Representative
- Standing Members
- Temporary Voting Members (TVM)

**Non-Voting Members**

- Industry Representative
- Consultants without permission to vote

# Open vs. Closed Session

## Open

- Majority of AC meetings are open to the public
- Any product approval meeting
- Every meeting must have a minimum of one hour scheduled for open public participation

## Closed

- Discuss trade secret/confidential information
- Non-public sponsor information; Personal/private information
- Must be approved by the Office of Commissioner

# Challenge Question 1

If your Type B meeting (non EOP) is granted, by when must you submit your meeting package?

A) At the time of the meeting request

B) No later than 30 days before the scheduled date of the meeting or WRO response time

C) No later than 50 days before the scheduled date of the meeting or WRO response time

D) No later than 47 days before the scheduled date of the meeting or WRO response time

# Challenge Question 2

Which expedited program features approval based on an effect on surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict drug's clinical benefit?

A) Priority Review

B) Accelerated Approval

C) Breakthrough Therapy

D) Fast Track

33

34