GDUFA III Redesigned Pre-Submission (PSUB) Meetings

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A Deep Dive: GDUFA III Scientific Meetings – May 15, 2023

Learning Objectives

- Clarify the purpose of the redesigned pre-submission (PSUB) meetings under GDUFA III
- Describe new GDUFA III timeline and changes to overall meeting goal and process
- Identify what, when, where, and how to submit your PSUB meeting request

Goals of Pre-ANDA Program

- Clarify regulatory expectations for prospective applicants early in product development
- Assist applicants in developing more complete submissions
- Promote a more efficient and effective ANDA assessment process
- Reduce the number of assessment cycles needed to obtain ANDA approval

Complex Products

Complex active pharmaceutical ingredient (API)	• Any drug product containing a complex API, regardless of administration routes and dosage forms. e.g., Conjugated Estrogen Tablet, Glatiramer Acetate Injection
Complex routes of delivery	• Any non-solution drug product with a non-systemic site of action (e.g., topical, ophthalmic, local gastrointestinal (GI) action) e.g., Cyclosporine Emulsion, Acyclovir Cream
Complex dosage forms/formulations	• Any non-oral complex formulation/dosage form product where there are often two or more discrete states of matter within the formulation e.g., Doxorubicin HCl Liposomes, Leuprolide Acetate for Depot Suspension
Complex drug-device combinations	• Where the drug constituent part is pre-loaded in a product-specific device constituent part or is specifically cross-labeled for use with a specific device, in which the device design affects drug delivery to the site of action and/or absorption e.g., Epinephrine Injection (autoinjector)
Other products	• Any solid oral opioid drug products with FDA approved labeling for that show properties (and thus gaining their labeling) to meaningfully deter drug abuse e.g., Hydrocodone Bitartrate ER Tablet

- *Lionberger R. Innovation for Generic Drugs: Science and Research Under the Generic Drug User Fee Amendments of 2012, Clinical Pharmacology & Therapeutics (CPT), 2019, Vol.105(4), p.878-885;*
- *GDUFA III Commitment Letter;*
- *MAPP 5240.10: Classifying Approved New Drug Products as Complex Products for Generic Drug Development Purposes (April 2022)*

Pre-ANDA Meetings

Pre-ANDA meetings were introduced in GDUFA II to facilitate pre-submission communications between the FDA and a prospective applicant related to a ***complex*** product and/or complicated drug development questions

- Product Development (PDEV) – No change from GDUFA II
- Pre-submission (PSUB) – *Redesigned for GDUFA III*

GDUFA: Generic Drug User Fee Amendments

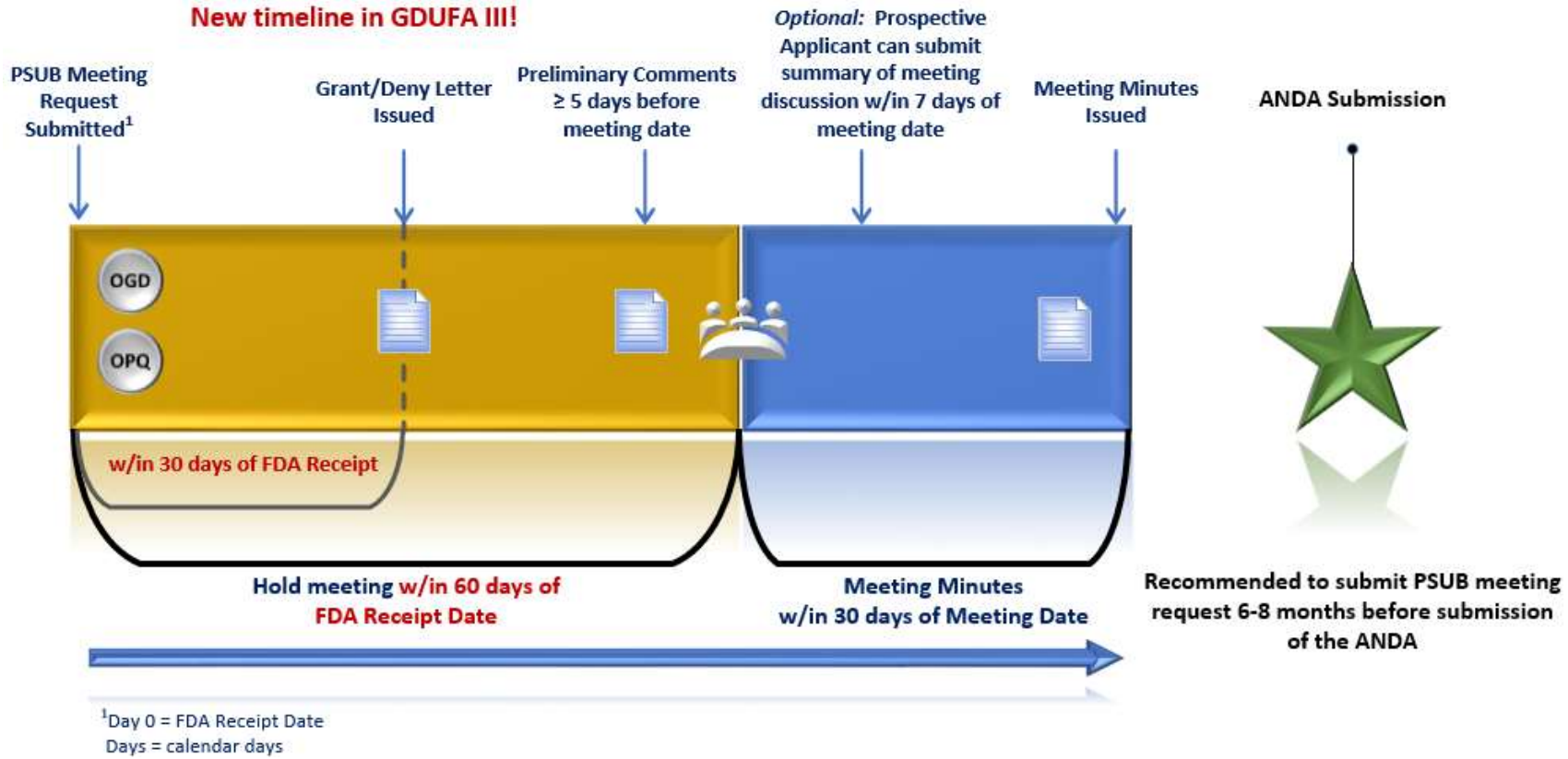
Purpose of Redesigned PSUB Meetings

- Provides a prospective applicant the opportunity to present ***unique*** or ***novel*** data or information that will be included in the ANDA submission, such as
  - Formulation
  - Key studies
  - Justifications
  - Methods used in product development
  - Interrelationship of the data and information in the ANDA
- ***DOES NOT*** include substantive assessment of summary data or full study reports
- ***IS NOT*** an opportunity to determine whether the ANDA is acceptable for receipt

PSUB Meeting Eligibility

- ✓ FDA ***will*** grant a PSUB:
  - If prospective applicant was granted a prior product development (PDEV) meeting for the same complex generic product
  - If FDA believes in its sole discretion that a PSUB meeting would improve assessment efficiency
    - Prospective ANDA applicants may request a PSUB meeting whether they had a PDEV meeting or not

PSUB Meeting Timeline



PSUB Meeting Package

- Refer to the “Formal Meetings Guidance” before submitting
- Submit concurrently with the PSUB meeting request
- In general, high-level information is sufficient
- In general, ***should not*** include questions

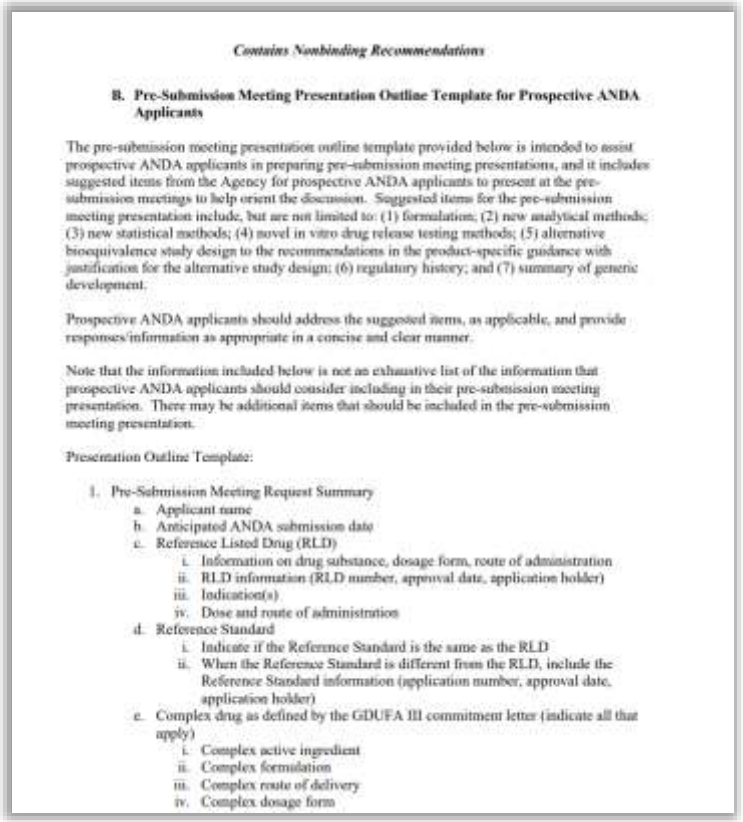
“Formal Meetings Guidance”: Guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*

PSUB Meeting Package

- Meeting package should include the following, among other items:
  - If there were any prior PDEV meetings for the same proposed complex generic product
    - Event IDs for the prior PDEV meeting(s)
    - Summary of the advice provided from PDEV meeting(s)
  - ***If no prior PDEV meeting(s) were held***, an explanation for why a PSUB meeting should be granted
  - Estimated timeline for submission of the ANDA
  - Unique or novel data or information to be included in the ANDA submission

PSUB Meeting Package

- PSUB meeting package can be submitted in the format of a draft meeting presentation
  - For a suggested presentation outline template with recommendations on information that should be included, see **Appendix B** of the "Formal Meetings Guidance"



Contains Nonbinding Recommendations

B. Pre-Submission Meeting Presentation Outline Template for Prospective ANDA Applicants

The pre-submission meeting presentation outline template provided below is intended to assist prospective ANDA applicants in preparing pre-submission meeting presentations, and it includes suggested items from the Agency for prospective ANDA applicants to present at the pre-submission meetings to help orient the discussion. Suggested items for the pre-submission meeting presentation include, but are not limited to: (1) formulation; (2) new analytical methods; (3) new statistical methods; (4) novel in vitro drug release testing methods; (5) alternative bioequivalence study design to the recommendations in the product-specific guidance with justification for the alternative study design; (6) regulatory history; and (7) summary of generic development.

Prospective ANDA applicants should address the suggested items, as applicable, and provide responses/information as appropriate in a concise and clear manner.

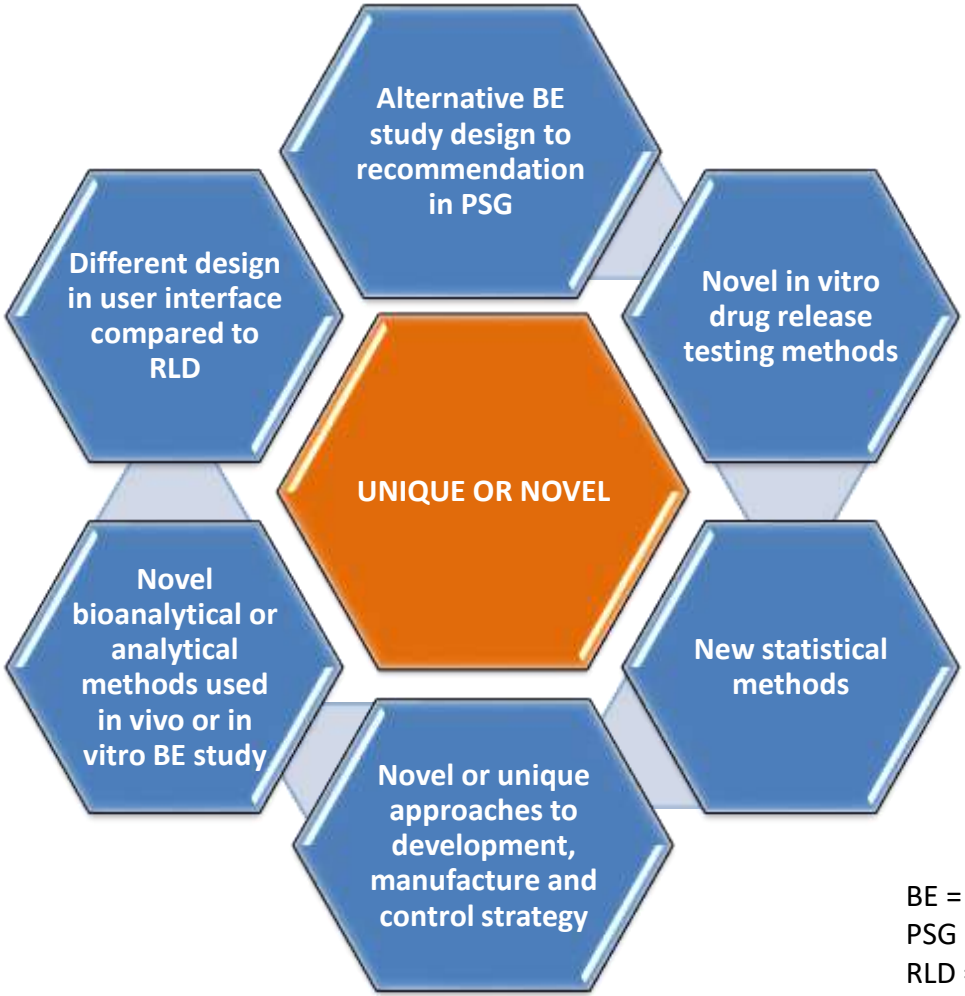
Note that the information included below is not an exhaustive list of the information that prospective ANDA applicants should consider including in their pre-submission meeting presentation. There may be additional items that should be included in the pre-submission meeting presentation.

Presentation Outline Template:

1. Pre-Submission Meeting Request Summary
   a. Applicant name
   b. Anticipated ANDA submission date
   c. Reference Listed Drug (RLD)
      i. Information on drug substance, dosage form, route of administration
      ii. RLD information (RLD number, approval date, application holder)
      iii. Indication(s)
      iv. Dose and route of administration
   d. Reference Standard
      i. Indicate if the Reference Standard is the same as the RLD
      ii. When the Reference Standard is different from the RLD, include the Reference Standard information (application number, approval date, application holder)
   e. Complex drug as defined by the GDUFA III commitment letter (indicate all that apply)
      i. Complex active ingredient
      ii. Complex formulation
      iii. Complex route of delivery
      iv. Complex dosage form

Refer to guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*

PSUB Meeting Package



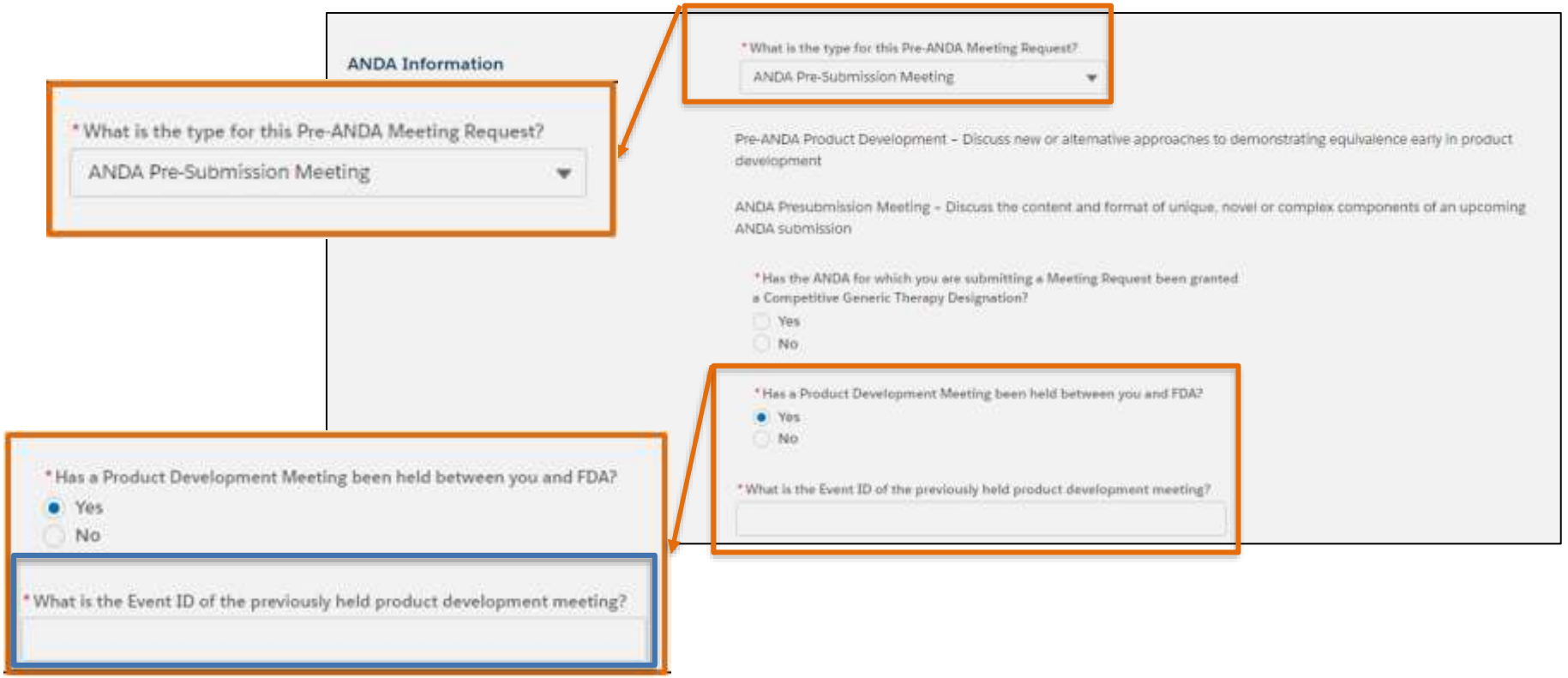
BE = Bioequivalence
PSG = Product-specific guidance
RLD = Reference listed drug

Submitting Your Meeting Request

- Obtain a pre-assigned ANDA number if no prior PDEV meeting
  https://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm114027.htm

- Submit via the CDER Direct NextGen Collaboration Portal
  https://edm.fda.gov

Submitting Your Meeting Request



Within 30 Days of Receipt

- Parallel grant/deny assessments performed by OGD and OPQ
  - Will reach one unified decision
- If granting, FDA will:
  - Identify ANDA assessment team members who will attend the PSUB meeting
  - In the grant letter, identify additional topics that prospective applicant should address during the meeting, when applicable
- If denying, FDA will provide the reason for denial
- By Day 30, issue grant/deny letter

Your Meeting Was Granted

- PSUB offered as in-person face-to-face (FTF) or videoconference meetings
  - As of March 27, 2023, prospective applicants can request in-person FTF meetings for PDEV or PSUB meetings
- If your request meets the criteria in the GDUFA III commitment letter, FDA will generally grant the requested meeting format
- Format of the meeting and scheduling information will be included in your grant letter
- A project manager (PM) from the Office of Research and Standards (ORS) will be your primary point of contact

Within 60 Days of Receipt

- FDA will generally not issue information requests for PSUB meetings
- Draft presentations may be updated ***up to 21 days*** prior to the meeting so that FDA may provide preliminary comments at least 5 days before the meeting date
  - Final presentations should be submitted ***at least 48 hours prior*** to the scheduled meeting date
- FDA will issue preliminary written comments no later than 5 days prior to the meeting date
  - FDA may indicate there are no comments
- Preliminary comments should not result in cancellation of a PSUB meeting
- By Day 60, PSUB meeting is held

In-Person Meetings

- ***At least 2 weeks prior to the scheduled meeting date*** provide the assigned PM:
  - Name, title, and company affiliation of all meeting participants
  - Relevant information (e.g., country of citizenship, passport information, etc.) for any Foreign National (FN) visitors participating in person
    - Foreign Visitor Data Request Form will be included with the Meeting Request Granted Letter (PSUB) or Meeting Information Letter (PDEV)
- ALL visitors must present a valid government-issued photo identification on the day of the meeting
  - FN visitors ***must*** present the passport that matches information provided to the PM or will be denied entry
  - Lawful Permanent Residents (LPR) of the U.S. ***must*** present a valid LPR card. Other forms of identification will not be accepted

Meeting Day

- Meetings are typically 60 minutes
- Prospective applicant's presentation will help orient the discussion
- FDA attendees will include:
  - Members of the ANDA assessment team
  - Participants in prior PDEV meetings, if applicable
- At the meeting, FDA will identify items or information that should be clarified before submission of the ANDA

Meeting Minutes

- If a prospective applicant would like FDA to consider their meeting summary:
  - Submit within 7 calendar days of the meeting via the portal
- FDA will issue meeting minutes within 30 calendar days after the meeting date
- FDA-issued minutes are considered the official record of the meeting

Dispute of Meeting Minutes

- A prospective applicant requesting additional clarification of the meeting minutes issued by FDA should contact the assigned FDA point of contact (POC)
- FDA recommends any concerns about the meeting minutes be submitted in writing to FDA within 10 calendar days of receipt

Challenge Question #1

FDA recommends that a pre-submission meeting request be submitted how far in advance of the ANDA submission?

A. 12 months

B. 6-8 months

C. 10-12 months

D. 2-3 months

Challenge Question #2

Which of the following statements is NOT true?

A. In GDUFA III, PSUB meetings provide prospective applicants the opportunity to present unique or novel data or information that will be included in the ANDA submission

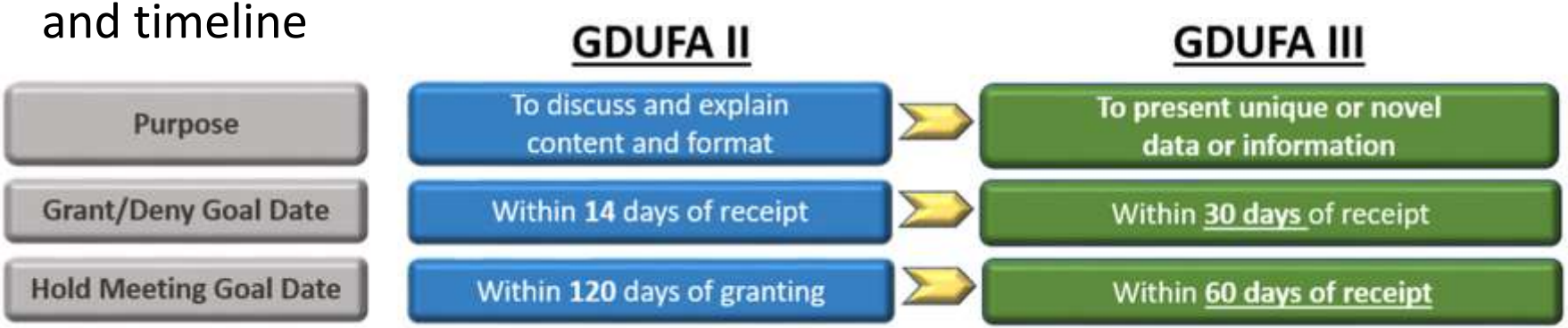
B. For a PSUB meeting, FDA will not provide a substantive assessment of summary data or full study reports

C. A PSUB meeting will be granted as a teleconference or written response only if requested by the prospective applicants

D. The meeting package for a PSUB meeting can be submitted in the format of a draft presentation

Summary

- PSUB meeting has been redesigned for GDUFA III with a new scope and timeline



- A request for a PSUB meeting should be made approximately 6-8 months before the ANDA submission
- Seek FDA's input via a PDEV meeting so that FDA has knowledge of your development program at the time of the PSUB meeting

Resources

- GDUFA Reauthorization Performance Goals And Program: Enhancements Fiscal Years 2023-2027 (GDUFA III Commitment Letter)
- Guidance for industry *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA* (October 2022)
- MAPP 5220.8 (Rev 1): *Evaluating Requests for and Conducting Product Development and Pre-Submission Pre-ANDA Meetings* (October 2022)
- Infographic: GDUFA III – Summary of Teleconferences and Meetings
- MAPP 5240.10: *Classifying Approved New Drug Products as Complex Products for Generic Drug Development Purposes* (April 2022)
- Draft guidance for industry *Controlled Correspondence Related to Generic Drug Development* (December 2022)
- GDUFA III Enhancement to the Pre-ANDA Program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