The GDUFA II Pre-ANDA Program for Complex Products

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What I’m Going to Cover

- Introduction to the Pre-ANDA meeting program
- Submitting a meeting request through the Portal
- The Pre-ANDA Process
- The Pre-ANDA Meeting Request and Package

The Pre-ANDA Program Goal

- The Pre-ANDA Program was established by GDUFA II
  - To clarify regulatory expectations for prospective applicants early in product development
  - Assist applicants to develop more complete submissions
  - Promote a more efficient and effective ANDA assessment process
  - Reduce the number of review cycles required to obtain ANDA approval, particularly for Complex Products

The Two Pre-ANDA Meeting Types

- Pre-ANDA meetings accelerate access to generics of complex products through early engagement with the FDA
  - Pre-ANDA Product development meetings (PDEV)
    - Early engagement in your individual product development program
  - Pre-Submission meetings (PSUB)
    - Ready to or close to submitting your application

Pre-ANDA Meeting Goal Dates

- Within 14 days FDA will respond to the request and grant or deny the meeting
- If a meeting is granted, FDA will offer a meeting date within 120 calendar days of granting the request
- Five days before the meeting you will receive preliminary written comments from FDA
- Meeting minutes will be sent 30 days after the meeting

Product Development Meetings

- A meeting involving a scientific exchange to discuss specific issues or questions
  - A novel proposed study design
  - Alternative bioequivalence approach
  - Additional study expectations
- FDA will provide targeted advice regarding an ongoing ANDA development program

Pre-Submission Meetings

- A meeting to discuss and explain the format and content of an ANDA to be submitted
- Applicants can obtain advice that will enable efficient review and improve the chance of first cycle approval
- Pre-submission meetings will not include substantive review of summary data or full study reports
- ANDA expected to be submitted within 6-12 months

Pre-ANDA Meeting Decision

- FDA will grant a prospective applicant a Product Development Meeting if, in FDA's judgment:
  - The meeting concerns development of a Complex Product for which FDA has not issued product-specific guidance or proposes an alternative equivalence evaluation (i.e., change in study type, such as in vitro to clinical) for a Complex Product for which FDA has issued product-specific guidance;
  - The prospective applicant submits a complete meeting package, including a data package and specific proposals;
  - A controlled correspondence response would not adequately address the prospective applicant's questions; and
  - A Product Development Meeting would significantly improve ANDA assessment efficiency.

Pre-ANDA Meeting Decision (cont.)

- A product development meeting may be granted if the meeting concerns complex product development issues other than those identified above (e.g., FDA has developed a product-specific guidance and the prospective ANDA applicant is not proposing an alternative equivalence evaluation), dependent on available resources, if:
  - The prospective applicant submits a complete meeting package, including a data package and specific proposals
  - A controlled correspondence response would not adequately address the prospective applicant's questions
  - A Product Development Meeting would significantly improve ANDA assessment efficiency

The CDER Direct NextGen Collaboration Portal

- Commonly called the “Portal”
- Use for pre-ANDA meeting requests for complex generic drug products
  - You will need a pre-assigned applicant number*
  - You will need a U.S. agent if you are a non-U.S. applicant
  - Pre-ANDA product development meetings
  - Pre-submission meetings

*Requesting a Pre-Assigned Application number

Create a Login for the Portal

- Once on the website, click Request a Login
- Choose Pre-ANDA Meetings as your “event”
- Register as either a U.S. agent or the applicant
- Enter the required information
- Once approved, you will receive your username and temporary password
- Login request will not be processed until you verify your email

Login FAQs

- My organization doesn’t appear when I search
  - You can enter it manually
- I don’t have a DUNS number or I don’t know what it is
  - Use the 9-digit code, 999999999
- Contact the EDM support team if needed at EDMSupport@fda.hhs.gov

U.S. Agents

- If you are submitting as a U.S. agent, fill in your applicant's information
  - Search for applicant information or enter manually
  - Provide the applicant contact information
- If you are the applicant, with no U.S. agent, proceed to "Attach a Document"
  - Do not enter yourself as a U.S. agent

My Login has been Created – Now What?

- Click “Create New Request”
- Enter required information
  - Pre-assignment number
  - What type of meeting request are you submitting
  - Reference Listed Drug (RLD)

Submitting Your Meeting Request

- Before you submit your request
  - You have the option of saving your draft meeting request
  - Come back to it later and continue where you left off
  - FDA cannot see saved meeting requests
- You can delete a meeting request if you have not yet submitted it
- You will be asked to review for accuracy
- Click “Submit to FDA”
- You will receive a confirmation message and email once you have submitted your request

Two-Way Communication

- Submit and receive documents through the Portal with email notification
- Advantage - All your documents and correspondence in one place

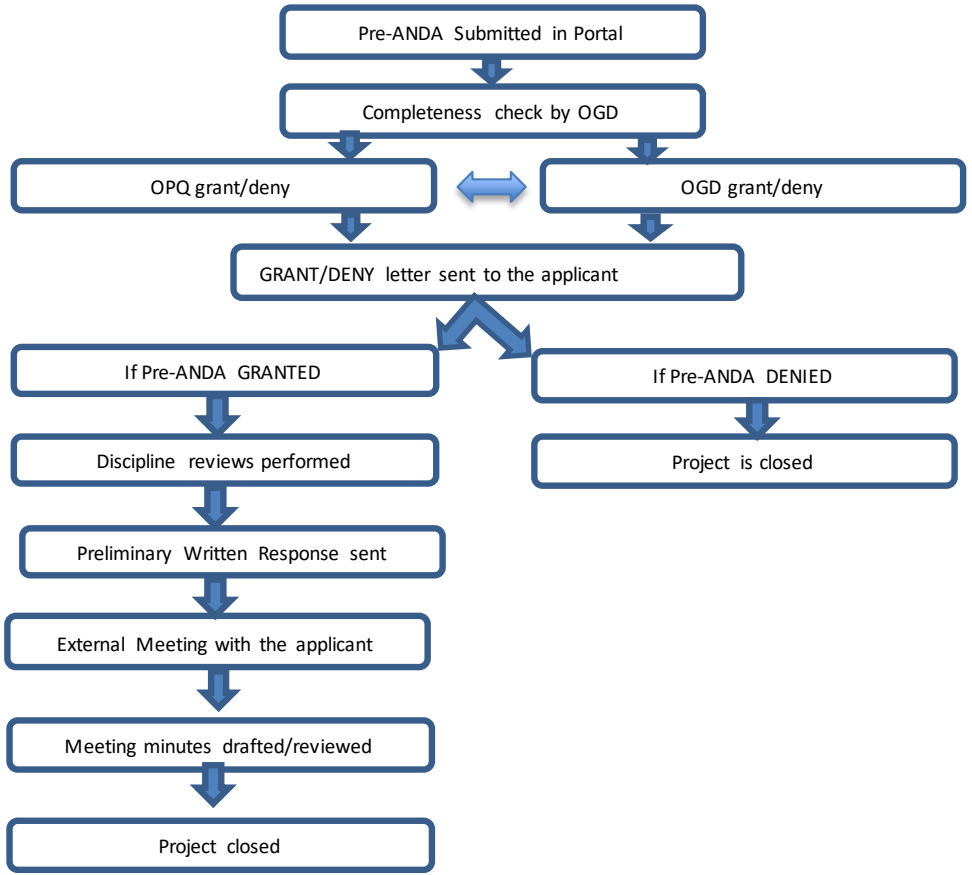
Adding Your Documents

- You must add a meeting package in order to proceed
- You can add more than one document
  - Cover letter
  - Meeting package (due at time of request for a meeting)
- Multiple formats allowed
  - PDF, Microsoft Word, Microsoft Excel, Microsoft PowerPoint, Microsoft Access, SAS, and Text
  - Macros are not allowed
  - Files may not exceed 45 MB

Grant/Deny Assessment

- Within 14 days, FDA will respond to the request and grant or deny the meeting
- If a meeting is denied, FDA will provide information to the applicant on a path forward
- If a meeting is granted, FDA will offer a meeting date within 120 calendar days of granting the request

Pre-ANDA PROGRAM OUTLINE



Phase 1 (14 days)

Phase 2 (120 days)

Phase 3 (30 days)

Meeting Package Format

- Refer to the draft guidance (Oct 2017)
  - *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA Guidance for Industry*
- Number your questions clearly and group them by discipline
  - e.g., Bioequivalence, CMC, etc.
- Minimize the use of sub-questions, for example a, b, c, etc.

https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm578366.pdf

Meeting Package Content: Product Development Meetings

- Provide clear and specific questions about your development program

- Include data supporting the proposed new approach that may include
  - Characterization of the RLD and ANDA products
  - Results from pilot studies
  - Comparisons of the proposed approach to that currently recommended by FDA
  - Quantitative analysis (PBPK, PK/PD, or BE simulation) that supports your approach

Meeting Package Content: Pre-Submission Meetings

- Outline the unique, novel or complex aspects of your upcoming submission that you will present at the meeting

- If you have specific questions, provide appropriate background material and data related to those questions

Meeting Request Evaluation

- Assessment team will evaluate Pre-ANDA meeting requests
  - Office of Generic Drugs (OGD) and Office of Pharmaceutical Quality (OPQ) perform separate triage functions to determine whether to grant/deny and the extent of participation
  - OGD and OPQ coordinate to provide a unified response
  - The assessment team reviews the product details, contents and submitted questions in the meeting package
  - The assessment team determines whether the meeting is granted or denied

What Happens Next?

- A letter with the grant or deny decision will be sent to you through the portal
  - A meeting denied letter will complete your project
    - You will be advised on the next steps, for example, submit a controlled correspondence instead

My Meeting Was Granted

- Typically granted as face-to face meeting, though the applicant can request a written response or teleconference
- Information Requests (IR)
  - Sent to the applicant through the Portal
  - Can be sent to the applicant at any time
  - FDA strives to send early in the process
  - Applicant responds to the IR through the Portal under the SAME event ID, not as a new meeting request.

Preliminary Responses

- Preliminary responses for face-to-face meetings and teleconferences will be sent through the portal approximately five days before your scheduled meeting
- Your opportunity to focus your meeting for clarification
  - Submit presentation materials (not required)
  - Submit a revised agenda
  - Submit these through the portal

  } Do not submit until after you have received your preliminary response
- You can cancel your meeting if you feel the preliminary responses adequately address your questions

Meeting Day

- Prospective ANDA applicant submits meeting slides and agenda via the Portal approximately 48 hours before
  - Meetings are typically 1 hour
  - Agenda should be focused on clarification or further discussion around the preliminary written comments

- Meeting participants discuss the data, questions, and the responses provided to assist the prospective ANDA applicant's complex product development program

- **FDA cannot review new material presented at the meeting for the first time**

After the Meeting

- The applicant can submit post meeting comments through the Portal
  - Within seven days of the meeting
- FDA will send the final meeting minutes through the Portal within 30 days of the meeting
- This completes the meeting request

Common Reasons for Denial

- Incomplete meeting packages
- Not a complex product
- Wrong meeting type chosen – PDEV vs PSUB
- Should be a controlled correspondence
- PSG is available and not asking for an alternate bioequivalence route

Am I a Pre-submission or Product Development Meeting?

- Product Development meetings are for discussion of specific scientific issues
  - Proposed study design, alternative approach, additional study expectations

- Pre-submission meetings are for 6-12 months before submission
  - You are ready to submit
    - Do you have your stability batches started?
  - Discuss format and content of ANDA
    - Not a filing review

Am I a Controlled Correspondence or a Meeting?

- Standard controlled correspondence (aka controls) reviewed in 60 days
  - Use for guidance clarification and rapid input into development programs
- Complex controls reviewed in 120 days
  - Clinical input (protocols for Safety determination letters)
  - Alternate BE approach (within the same class)
- Complex control expands what we can consider via the control process
- Meetings are best for multidisciplinary questions
- Controls are for single questions or a small group of closely related questions

Examples of Unclear Questions

- Is my PK study acceptable?
  - Instead identify the point of uncertainty and ask a specific question
- Is my specification acceptable?
  - Instead ask a specific question about this complex product and your understanding of how you will control the CQA of your product
- Do not submit a protocol and ask us to review it
  - Instead submit specific questions regarding your protocol

Questions

- Are product development meetings good for broad questions?
  - No, you should provide specific questions and include justification.
- Should I submit my entire protocol for comment?
  - No, again, specific questions with data other justification.

Questions?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