GDUFA II Pre-ANDA Program Meetings: Advice for Success

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Generic Drug Forum

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Agenda

- Introduction to the Pre-ANDA (PANDA) program

- Pre-ANDA Process
  - Industry
  - FDA/OGD
  - FDA/OPQ

- Tips on preparing your Pre-ANDA Meeting Request and Package

The Pre-ANDA Program

- The Pre-ANDA Program was established by GDUFA II
  - Goal: 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, and reduce the number of review cycles required to obtain ANDA approval, particularly for Complex Products

- Pre-ANDA meetings accelerate access to generics of complex products through early engagement with the FDA
  - Product development meetings
  - Pre-Submission meetings
  - Mid-review cycle meetings

Complex Products

COMPLEX…	Example	Example Products
Active ingredients	Peptides, complex mixtures, natural source products	Glatiramer acetate
Formulations	Liposomes, emulsions, sub-lingual films	Liposomal formulation
Routes of Delivery	Locally acting drugs such as dermatological products and complex ophthalmological products	Acyclovir cream
Dosage Forms	Transdermal systems, extended release injectables	PLGA microspheres
Drug-Device Combinations	Dry powder inhalers, nasal sprays, enteric feeding tubes	Mometasone
Other products	Complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement	Abuse deterrent opioid formulations

Product Development Meetings

- A meeting involving a scientific exchange to discuss specific issues or questions
  - E.g., a proposed study design
  - Alternative 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

- Pre-submission meetings will not include substantive review of summary data or full study reports

- ANDA expected to be submitted within 6-12 months

PANDA Meetings

- 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
  - The prospective ANDA applicant 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;
  - A Product Development Meeting would significantly improve ANDA assessment efficiency.

PANDA Meetings

- 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:
  - 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

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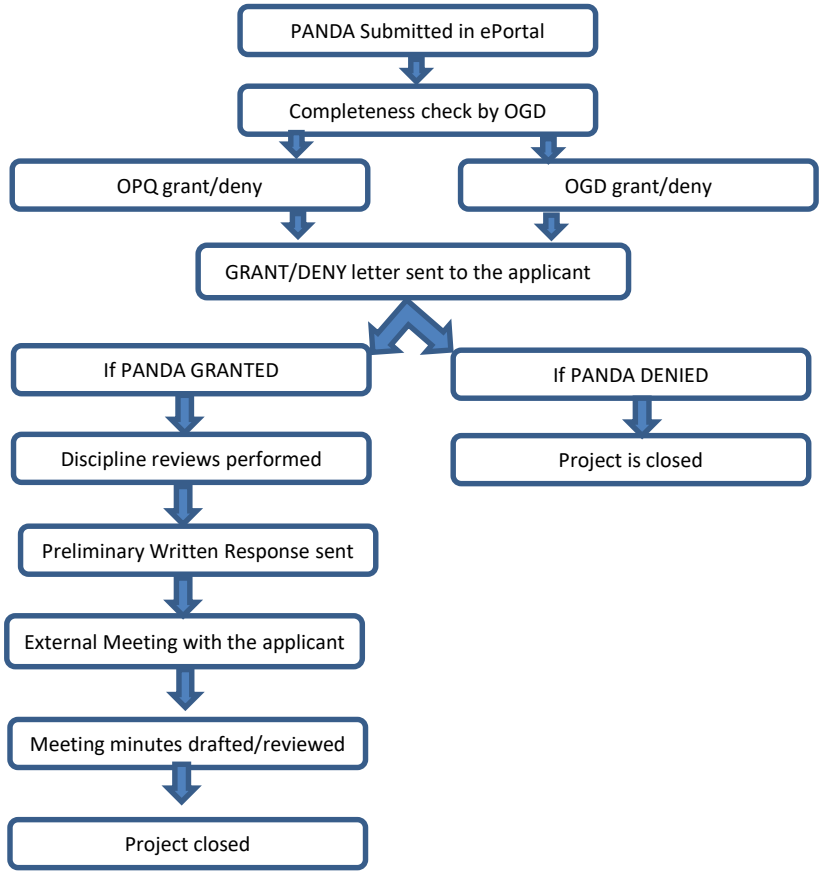
Pre-ANDA PROGRAM OUTLINE



Submitting Your Meeting Request

- Obtain a pre-assigned ANDA number before requesting the meeting
  - Pre-assigned numbers do not expire
  - Register on the portal as either a US agent or as the applicant

- Use CDER Direct NextGen Collaboration Portal (the Portal) to submit the meeting request
  - https://edm.fda.gov

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 Request Evaluation

- FDA will evaluate PANDA meeting requests
  - OGD and OPQ perform separate triage functions to determine grant/deny and the extent of participation

- Within 30 days (year one and two) or 14 days (year three and beyond) 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

Meeting Package Review

- A project manager from the Office of Research and Standards (ORS) is assigned as a point of contact
- FDA staff will review the meeting package, request consults if needed, and send information requests
  - Prospective ANDA Applicant responds to any IRs via the Portal
- FDA will strive to send preliminary written responses five days prior to the meeting

FDA Staff Roles (OGD)

- Division Level Signatory
  - An ORS division director or deputy who makes the decision to grant and oversees the meeting process
  - Accountable for the accuracy and completeness of the response
- Meeting Project Manager
  - Point of contact for industry
  - Facilitates internal meeting preparation, consults and information sharing
- Meeting Team Leader
  - Responsible for coordinating all discipline reviews into a consistent response

FDA Staff Roles (OPQ)

- OPQ Triage Team
  - An OPQ team that is responsible for determining grant/deny for meeting requests and the extent of OPQ participation, if any
  - Responsible for assigning OPQ disciplines to meeting package review
- OPQ Disciplines
  - Drug substance, drug product, process and facilities, microbiology, biopharmaceutics, research
  - Responsible for answering discipline-specific questions
- OPQ Meeting Team Leader
  - Responsible for coordinating all OPQ discipline reviews into a consistent response

Meeting Day

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

- Meeting participants discuss the questions and the data 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**

Post-Meeting

- FDA will issue official minutes within 30 days of the meeting

- If you would like FDA to consider your meeting summary
  - Submit within 7 days of the meeting
  - Can be submitted via the portal

Pre-ANDA Continuity

- For pre-submission meetings, FDA will identify representatives of the ANDA review team to participate in the meeting

- For pre-submission meetings and subsequent ANDA submissions, FDA will communicate the results of the product development meeting or other pre-ANDA interactions to the review team

- FDA conducts regulatory research to inform the review of complex drug products

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GDUFA II Pre-ANDA Metrics

- Six months into the program, 31 pre-ANDA meeting requests have been submitted

- 16 have been granted, 15 denied
  - Denied meetings are given a path forward, such as re-submit as a control or re-submit your meeting request with the following information (inadequate meeting package)

Tips Based on What We've Seen So Far

- Provide sufficient data to review question in the meeting package
- Q1/Q2 questions where not required by regulation—yes this is the pathway
  - Submit a meeting request that proposes a BE approach for a specific formulation
  - FDA will provide feedback on the BE approach
- Read the guidance on Comparative Analyses and Related Comparative Use Human Factors Studies for a Drug-Device Combination Product Submitted in an ANDA
  - Posted in January 2017
  - AKA: Comparative Analyses Guidance

https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536959.pdf

Am I a Pre-sub or Prod-dev 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 Prod-Dev?

- Standard controls reviewed in 60 days
  - Use for guidance clarification and rapid input into development programs
- Complex controls reviewed in 120 days (new in GDUFA II)
  - Clinical input (protocols for Safety determination letters)
  - Alternate BE
- Complex control expands what we can consider via the control process
- Clarification of ambiguities are allowed

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

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 Day!

- 5 days before the meeting you will receive preliminary written comments from FDA
  - Use these to optimize your meeting agenda

- Meeting minutes will be sent 30 days after the meeting

Conclusions

- Use the Portal to submit your meeting requests
- Read the guidance about submitting meeting requests to OGD
- Use correct pathway designation
  - Product Development, Pre-Submission, or Controlled Correspondence
- Provide sufficient information


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