U.S. FOOD & DRUG ADMINISTRATION

Overview of Pre-ANDA Meeting Program

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Learning Objectives

- Pre-ANDA meeting types and formats
  - Main focus: product development pre-ANDA meeting
- Controlled Correspondences
- Best practices in preparing the meeting package
- Other pre-submission communications

Pre-ANDA Meeting Program

Pre-ANDA meetings were introduced in GDUFA II to facilitate pre-submission communication with the FDA and a prospective applicant preparing to submit an abbreviated new drug application (ANDA) for a complex product and other complicated drug development questions

What is a Complex Product?

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.

Pre-ANDA Meeting Program

3 meetings under pre-ANDA meeting program

- Pre-ANDA phase
  - Product-Development Meeting (PDEV)
  - Pre-Submission Meeting (PSUB)
- After ANDA submission
  - Mid-Review Cycle Meeting (MRCM)

Meeting Types: Before ANDA Submission

Product Development (PDEV)

- Scientific exchange to discuss specific issues or questions (e.g., a proposed study design, alternative approach, or additional study expectations)
- Targeted advice regarding ongoing ANDA development program
- Prospective ANDA applicants may request more than one product development meeting

Pre-submission (PSUB)

- Discuss and explain content and format of the ANDA to be submitted
- Advice to enable efficient review and improve chances of first cycle approval
- Does ***not*** include substantive review of summary data or full study reports
- ANDA is anticipated to be submitted ~6 months of meeting date

Product Development Meetings

Will be granted if:

- The meeting concerns (1) development of a complex product for which FDA has not issued a product-specific guidance or (2) an alternative equivalence evaluation is proposed;
- The request contains a complete meeting package
- A controlled correspondence would not adequately address the prospective ANDA applicant's questions; and
- The meeting would significantly improve ANDA review efficiency

May be granted if, in FDA's judgment, the request concerns complicated product development issues even for non-complex products.

Controlled Correspondence (CC)

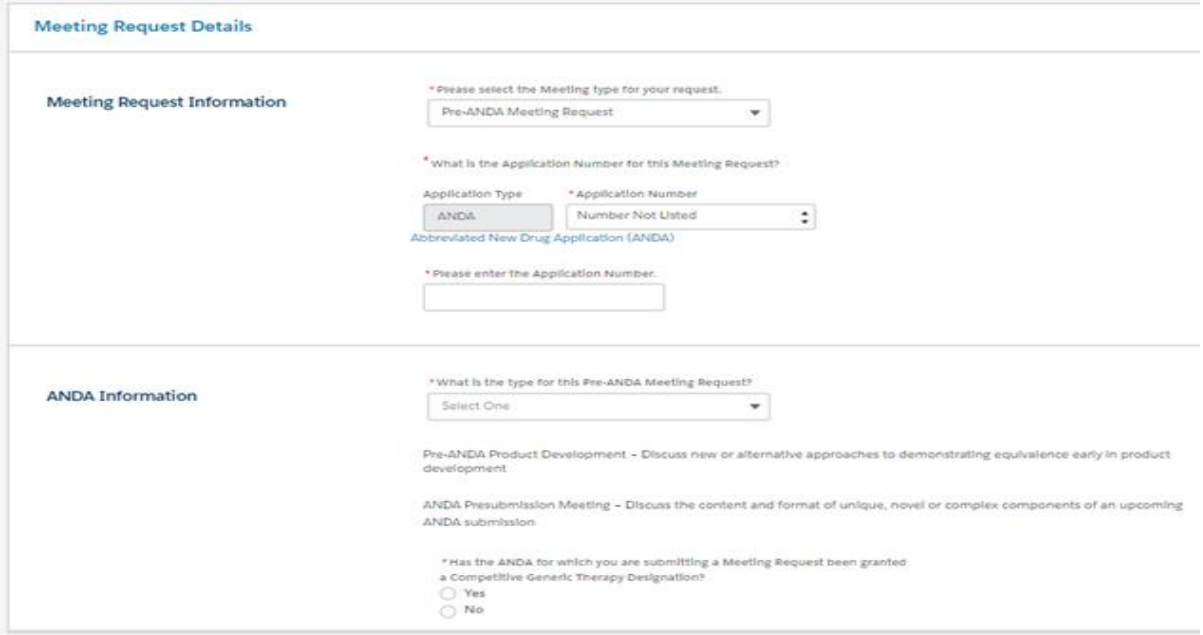
- **Standard CC (60 calendar days)**
  - Requesting information on specific element of generic drug development
  - Post approval submission requirements not covered by guidance on post approval changes and not specific to an ANDA
- **Complex CC (120 calendar days)**
  - Evaluation of clinical content
  - Bioequivalence (BE) protocols for reference listed drugs (RLDs) with risk evaluation and mitigation strategies (REMS) with elements to assure safe use (ETASU)
  - Alternate BE approach within the same study type (e.g., pharmacokinetic, in vitro, and clinical)

CC or PDEV Meeting?

- **Controlled Correspondence**
  - Single or a small group of closely related questions
  - Following a PDEV meeting, applicant seeking further clarification or has new question related to what was discussed at the meeting
  - Response within 60 (standard) or 120 (complex) calendar days
- **Pre-ANDA Meeting**
  - Best for multidisciplinary questions
  - New information, data, or questions that will not be adequately addressed in a controlled correspondence
  - Meeting held within 120 days of being granted
  - Recommend no more than one request for a product development meeting for the specific complex product per year

Submitting Your Meeting Request

- Obtain a pre-assigned ANDA number
  https://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm114027.htm
- Submit via the CDER Direct NextGen Collaboration Portal



Submitting Your Meeting Request

- Meeting package for PDEV
  - Provide specific proposals and questions supported by appropriate data and scientific justification
- Meeting package for PSUB
  - Outline the unique, novel, or complex aspects of your upcoming submission
  - If you have specific questions, provide appropriate background material and data related to those questions

Meeting Package Format and Content

- Refer to the final Guidance for Industry (November 2020)

  Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA Guidance for Industry
- Each question is followed by a corresponding justification, rationale or data to support discussion as applicable
- List of questions grouped by discipline (e.g., BE, Chemistry, Manufacturing, and Control (CMC), etc.)
- Each question clearly numbered (e.g., 1,2,3 without sub-questions)

More Tips

- Before submitting, read all applicable guidances and standards
- Ask specific questions about your development plan, proposed approach/method, study design, etc.
- Provide proper justification and preliminary data (as needed) to support your proposals
- No data dumping
- Do not ask review issues (e.g., acceptance criteria for specification, acceptability of the study results, etc.)

Proposed Formats of Meetings

- Written response,
- Teleconference, or
- Face-to-face (FTF)*

*see next slide for details on FTF meetings in the current situation

Face-to-Face Meetings

- Face-to-face pre-ANDA meetings currently are being conducted as Zoom meetings with video
- There is a differentiation between Zoom meetings and the “call only” T-con, which is voice only and no presentation needed

Your Meeting Was Granted

- A Project Manager from the Office of Research and Standards (ORS) or OPQ is assigned as the point of contact
- Will grant: Typically defaults to whatever format requested in meeting package given all criteria are met
- May grant: FDA will select most appropriate format
- Format of meeting will not impact whether you qualify for a MRCM. Same case if you cancel your meeting after receiving your preliminary responses.

Pre-ANDA Meeting Package Assessment

- After the meeting is granted, FDA staff will review the meeting package, request consults and send information requests (as needed)
- Information Requests (IR)
  - Sent to prospective applicant through the portal
  - FDA strives to send early in the process, but can be sent at any point
  - Prospective applicant responds to the IR via the portal
- Preliminary responses are based upon the Agency's current thinking and knowledge
  - May change with available data or research, etc.

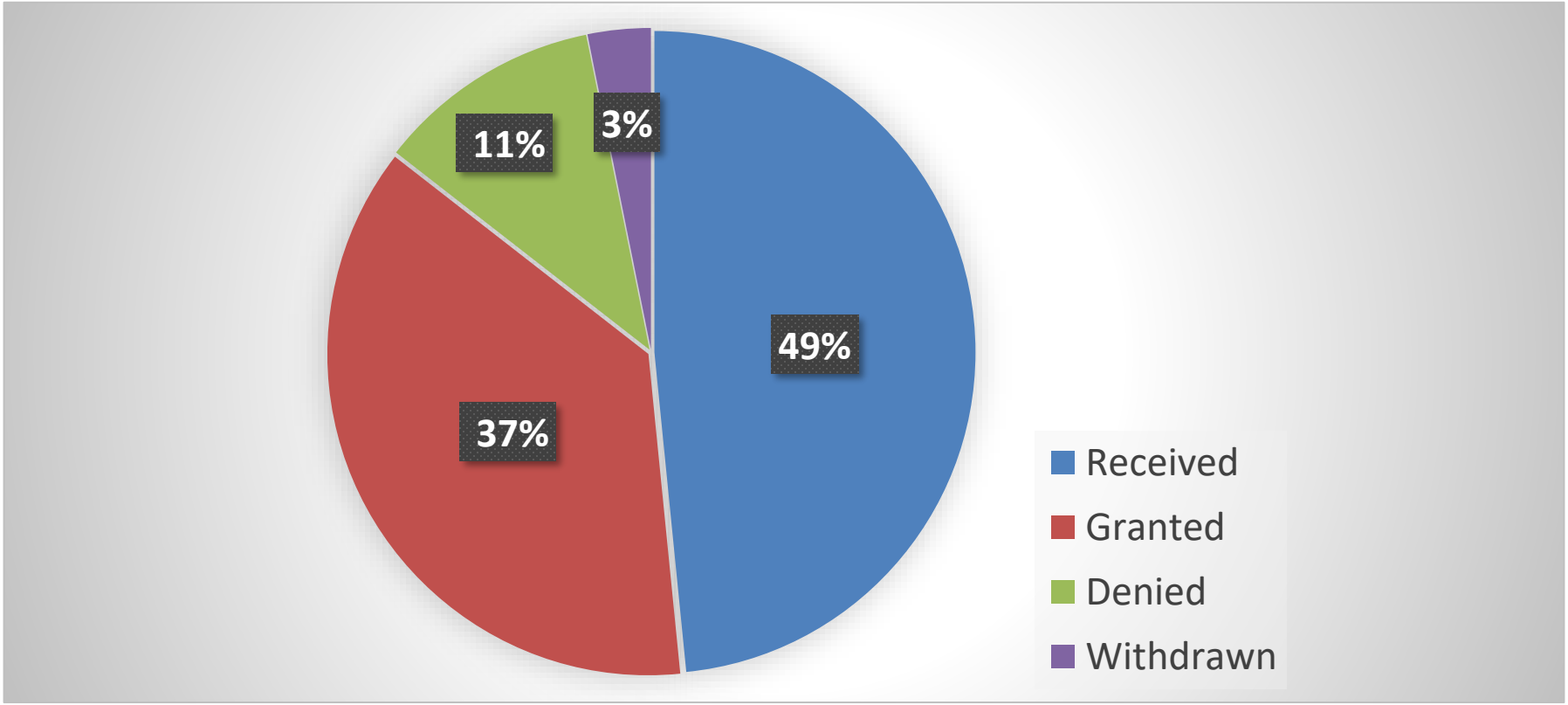
Preliminary Responses

- Preliminary written comments will be sent via the portal approximately 5 calendar days before your scheduled meeting
- Your opportunity to focus your meeting
  - Submit presentation materials (not required)
  - Submit a revised agenda
  - Submit these through the portal at least 48 hours prior to scheduled meeting
- Should NOT generate the submission of new questions
- You can cancel your meeting if you feel the preliminary responses adequately address your question

Meeting Day

- Meetings are typically 1 hour long
- Discussion should focus on clarification of the Agency's 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 **will not** address or discuss new data or questions not presented in the original meeting package

Pre-ANDA Meetings Received in FY 2021



Parallel Scientific Advice (PSA) Pilot

- A new pilot launched in Sept 2021
- EMA and FDA established PSA for applicants developing hybrid/complex generic products to jointly exchange agencies' views on scientific questions
- Scope:
  - For example, the applicant may use the PSA program to determine whether a study design(s) might be acceptable to both regulatory agencies.
  - Studies that may benefit from the PSA process include comparative non-clinical and comparative clinical studies involving innovative bioequivalence study designs and the use of methodologies such as modelling and simulation.
- Voluntary, not a GDUFA meeting
- Refer to the PSA principles document for more information
  - Accessed via the Office of Generic Drugs Global Affairs website: https://www.fda.gov/drugs/generic-drugs/global-generic-drug-affairs

Challenge Question 1

Which type of pre-ANDA meeting does ***not*** include substantive review of summary data or full study reports?

a. Pre-Submission Meeting
b. Product Development Meeting
c. MRCM

Challenge Question 2

Which one of the following factors will NOT grant a prospective applicant a Product Development Meeting?

a) Development of a complex product
b) Incomplete meeting package
c) CC will not adequately address question
d) PSG unavailable

Helpful Resources

- **MAPP 5220.8:** Evaluating Requests for and Conducting Product Development and Pre-Submission Pre-ANDA Meetings
- GDUFA II Commitment Letter
- **FDA Guidance for Industry:** Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA Guidance for Industry (Nov 2020)
- **FDA Guidance for Industry:** Controlled Correspondence Related to Generic Drug Development Guidance for Industry (Dec 2020)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