GDUFA II: Pre-ANDA Program and Meetings for Complex Generic Products

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Outline

- Overview of the pre-abbreviated new drug application (pre-ANDA) program
- Pre-ANDA meeting process
- Program metrics and trends
- Tips for success

Pre-ANDA Program Goals

- 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

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

www.fda.gov

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 Program Components

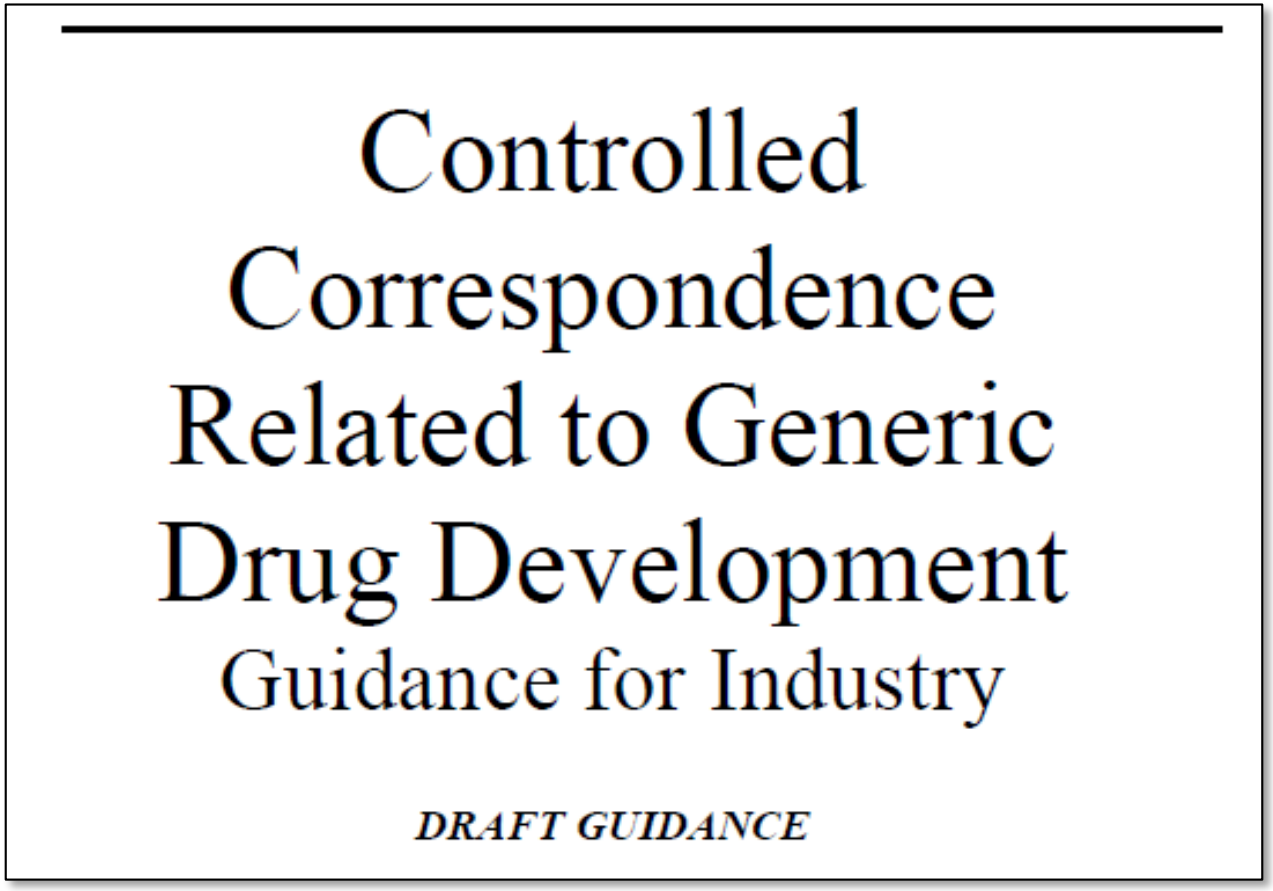
- Research
- Product-Specific Guidances (PSGs)
- Controlled Correspondence
- Meetings for ***complex*** products

Product-Specific Guidances (PSGs)

- Agency's current thinking and expectations on how to develop generic drug products therapeutically equivalent to specific reference listed drugs

- Approximately 1700 PSGs are currently available as of July 2019
  https://www.fda.gov/drugs/guidances-drugs/product-specific-guidances-generic-drug-development

- Upcoming New or Revised PSGs for Complex Generic Drug Product Development
  https://www.fda.gov/drugs/guidances-drugs/upcoming-product-specific-guidances-complex-generic-drug-product-development


Controlled
Correspondence
Related to Generic
Drug Development
Guidance for Industry
DRAFT GUIDANCE

Controlled Correspondence (CC)

- **Standard CC (60 calendar days)**
  - Specific element of generic drug development
- **Complex CC (120 calendar days)**
  - Clinical content
  - Bioequivalence (BE) protocols for 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)
- **Clarification of ambiguities (14 days)**
  - Submit within 7 days of reviewing FDA's response

GDUFA II Meetings: 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

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 study reports
- ANDA is anticipated to be submitted ~6 months of meeting date

GDUFA II Meetings: After ANDA Submission

Mid-Review-Cycle Meeting (MRCM)

- For applicants with prior PDEV and/or PSUB meetings
- Generally mid-point of review plus 30 days
- Update on status of review and next steps

CC or PDEV Meeting?

- Controlled Correspondence
  - Single or small group of closely related questions
  - Response within 60 (standard) or 120 (complex) calendar days
- Pre-ANDA Meeting
  - Best for multidisciplinary questions
  - Meeting held within 120 days of being granted

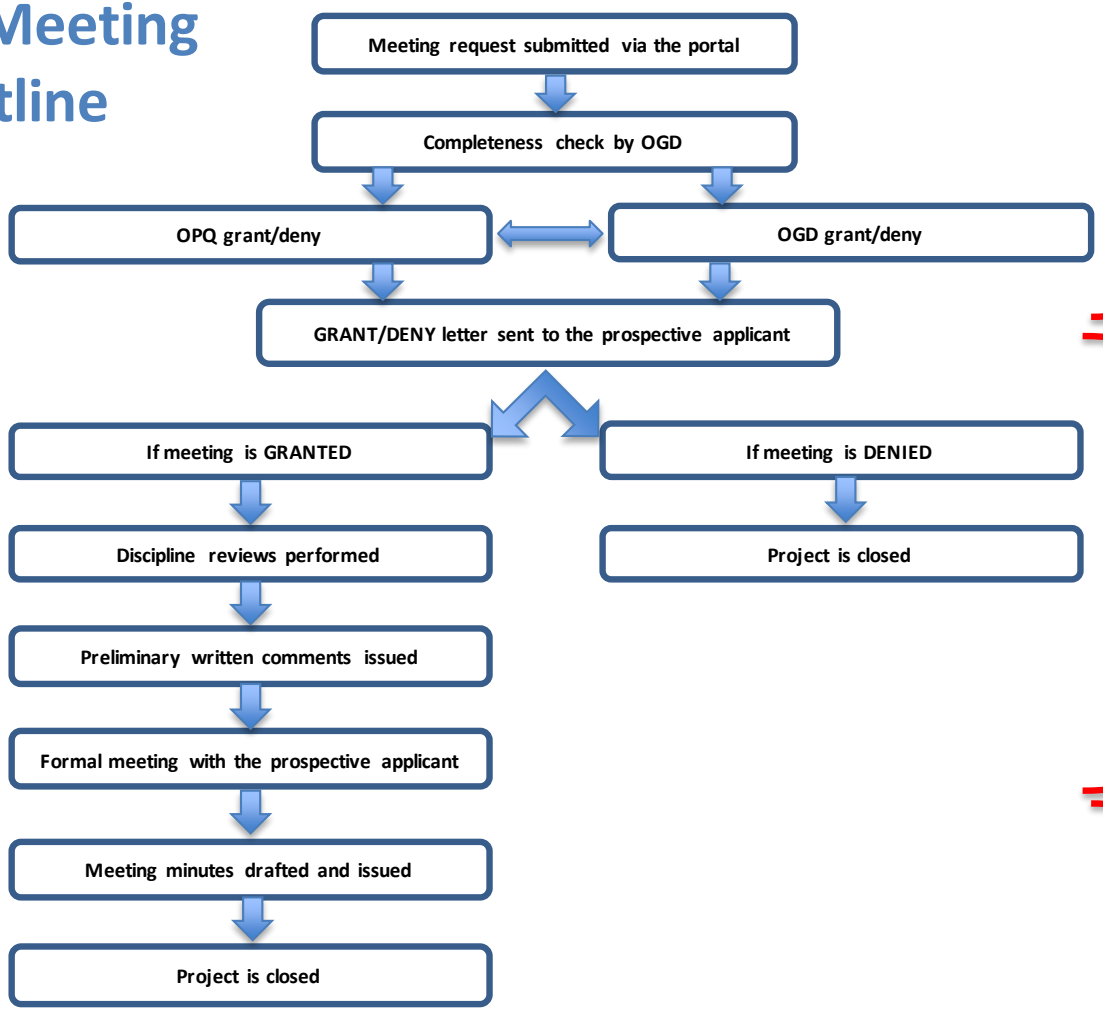
FDA will grant a PDEV or PSUB meeting for a complex product, if:

- No PSG available
- Proposing an alternative BE approach to the PSG
  - Change in study type (e.g., in vitro instead of in vivo approach)
- Meeting package is complete
- Questions could not be adequately addressed through a CC
- A meeting would significantly improve ANDA review efficiency

Depending on available resources, FDA may grant if, in FDA's judgment:

- Concerns complex product development issues
- Meeting package is complete
- Questions could not be adequately addressed through a CC, and
- A meeting would significantly improve ANDA review efficiency

Pre-ANDA Meeting Process Outline



Stage 1
(14 days*)
***As of Oct 1st 2019**

Stage 2
(120 days)

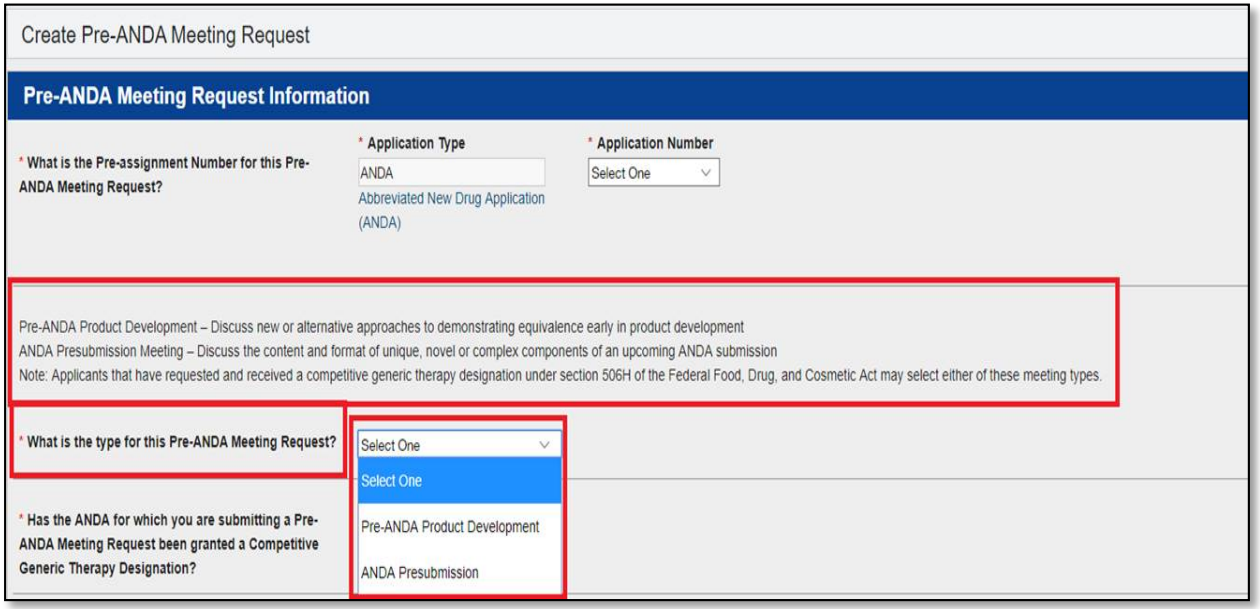
Stage 3
(30 days)

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 draft Guidance for Industry (October 2017)
  - *Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA*
- 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, CMC etc.)
- Each question clearly numbered (e.g., 1,2,3 without sub-questions)

Meeting Request Evaluation

- Parallel assessments of the meeting request by Office of Generic Drugs (OGD) and Office of Pharmaceutical Quality (OPQ)
  - Assessment team reviews the product details, contents and submitted questions
  - OGD and OPQ coordinate to provide a unified response

My Meeting Was Granted

- Typically granted as face-to face meeting, though the applicant can request a written response or teleconference
- Written responses and teleconferences still qualify you for a mid-review-cycle meeting
- A project manager from the Office of Research and Standards (ORS) is assigned as the point of contact

Pre-ANDA Meeting Package Assessment

- FDA staff will review the meeting package, request consults and send information requests (if 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
  - Applicant responds to the IR through 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 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 questions
  - Still be eligible for a MRCM

Meeting Day

- Meetings are typically 1 hour
- Discussion should be focused 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**

Post-Meeting

- If prospective ANDA applicants would like the FDA to consider their meeting summary:
  - Submit within 7 calendar days of the meeting via the portal
- FDA will issue official minutes within 30 calendar days of the meeting

Competitive Generic Therapy

- New pathway for drugs with "inadequate generic competition"

- Eligible for PDEV and PSUB meetings
  - Includes both complex and non-complex products
  - Provide documentation of Competitive Generic Therapy designation with meeting request
  - Does **not** provide for an expedited meeting timeline

- FDA will consider the following, among other factors, to determine whether to grant or deny a meeting request with CGT:
  - Complexity of developing an ANDA for a specific drug
  - Potential public health impact (e.g., severity of the condition treated, size of impacted patient population)
  - Impact on FDA resources and other workload commitments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