GDUFA II Pre-ANDA Program Meetings for Complex Products

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AAM Fall Technical Meeting

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GDUFA II Pre-ANDA Program Goals

- Clarify regulatory expectations for prospective applicants early in product development
- Help applicants develop more complete submissions
- Promote a more efficient and effective review process
- Reduce the number of review cycles necessary to obtain ANDA approval of complex products

Enhanced pre-ANDA Process in GDUFA II

Complex Products

- Early Stage
  - Regulatory Science
  - Pre-ANDA meetings with goals
- Mid-stage
  - BE guidance when available
  - Pre-ANDA meetings with goals for alternatives to BE guidance (different class)
  - 120 day controls for alternatives to BE guidance (same class)
- Submission and review
  - Pre-submission meeting with goals
  - Mid-cycle meetings

Non-complex Products

- Early Stage
  - Goals on BE guidance for New Chemical Entity (NCE; 2 years after NDA)
- Mid Stage
  - 60 day controls
  - 120 day controls for alternatives to BE guidance
  - IID enhancements
- Submission and review
  - Priority review when applicable

GDUFA II Pre-ANDA Program

- New meetings to accelerate access to generics of complex products
  - Product development meeting
  - Pre-submission meetings
  - Mid-review-cycle meetings

Draft Guidance on pre-ANDA Meetings
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM578366.pdf

Product Development Meeting Goals

- **Scientific exchange** on specific issues (e.g., a proposed study design) or questions
- **Targeted advice from FDA** for an ongoing ANDA development program

Pre-Submission Meeting Goals

- Provide an opportunity for the applicant discuss and explain content and format of the ANDA to be submitted
- Provide an opportunity for FDA to give advice that will enable efficient review and improve the chance of first cycle approval
  - Identify items or information for clarification before submission
- Allow FDA to share information from product development meetings with the ANDA review team and prepare for unique review issues

Eligibility

- FDA **will** grant Product Development Meetings if
  - The request concerns development of a **complex product** for which
    - FDA has not issued a product specific guidance or
    - The applicant proposes an alternative bioequivalence method of a different class
  - The request contains a complete meeting package including data and specific proposals
  - A controlled correspondence would not adequately address the questions
  - The meeting would significantly improve ANDA review efficiency

Eligibility

- FDA **will** generally grant Pre-Submission Meetings
  - If you were granted a Product Development meeting after October 1, 2014
- FDA **may** grant Pre-Submission Meetings
  - if in FDA's judgment the pre-submission meeting would improve review efficiency

Complex Drug Products In GDUFA II

- "Complex Product" is a defined term in the GDUFA II Commitment Letter.
  - Complex active ingredients
  - Complex formulations
  - Complex routes of delivery
  - Complex dosage forms
  - Complex drug-device combination products
  - Other products where complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement.

GDUFA II commitment letter. http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

Complex Drug Products In GDUFA II

- Non complex
  - tablet, capsules, solutions, and suspension for oral administration and systemic delivery
    - Solid oral modified release dosage forms are non complex
  - Solutions for topical or parenteral administration
- Complex active ingredients
  - Peptides, polymeric compounds, complex mixtures of APIs, naturally sourced ingredients
  - Larger peptides (> 6-8 AA)

Complex Drug Products In GDUFA II

- Complex formulations
  - Liposomes, colloids
- Complex dosage forms
  - Transdermal, metered dose inhalers, extended release injectables

Complex Drug Products In GDUFA II

- Complex routes of delivery
  - Locally acting drugs such as dermatological products and complex ophthalmological products and otic dosage forms that are formulated as suspensions, emulsions, or gels
  - Other routes including inhalation, nasal, GI acting

Complex Drug Products In GDUFA II

- Complex drug-device combination products (e.g., auto injectors, nasal spray, metered dose inhalers)
  - Not all combination products are GDUFA II complex products
  - Only the complex combination products are GDUFA II complex products
  - Complex combination products are those that have the potential for user interface differences the could impact successful substitution
    - Dry Powder Inhalers

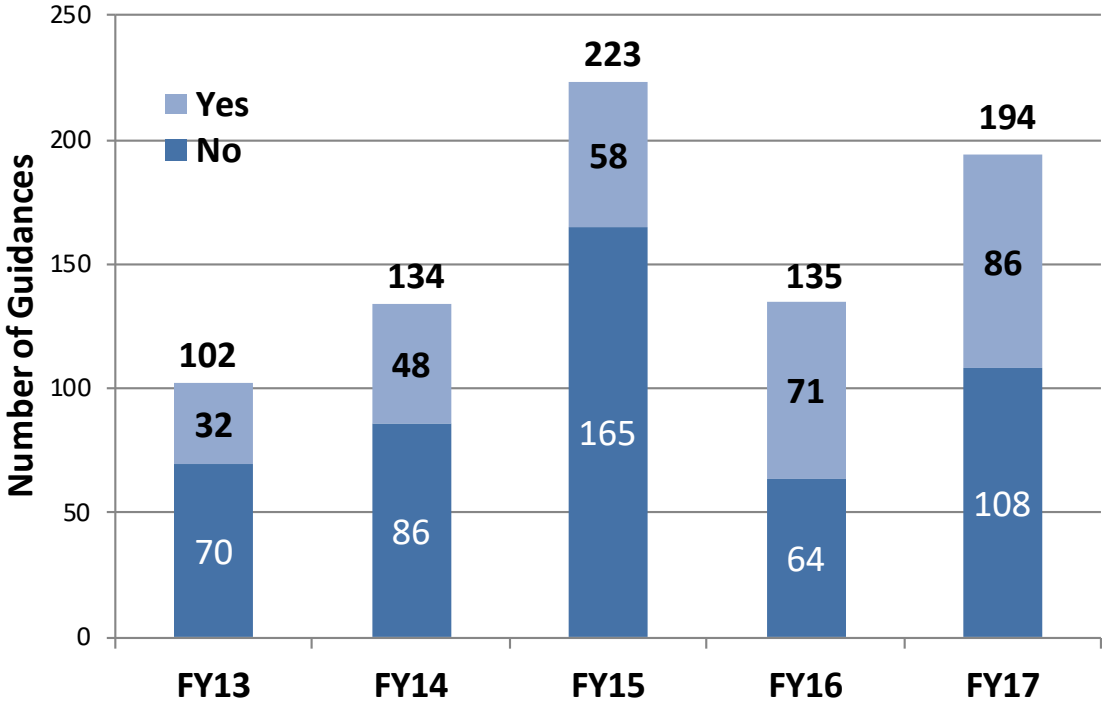
Complex Drug Products In GDUFA II

- Other products where complexity or uncertainty concerning the approval pathway or possible alternative approach would benefit from early scientific engagement
  - Abuse deterrent formulations
  - Non Q1-Q2 locally acting solutions not eligible for a biowaiver

Topics for pre-ANDA Meetings

- 127 pre-ANDA meeting packages reviewed in GDUFA I
  - No commitment in GDUFA I, mostly written responses
- Top categories
  - 35 on nasal/inhalation products
  - 31 on complex formulations
  - 25 on complex active ingredients
  - 10 on topical/transdermal
  - 8 on GI acting drugs
  - 8 on drug-device combinations

Product-Specific Guidances Increasing for Complex Products



GIDUFA II Guidance Commitments

- For NCE NDAs (non-complex)
  - FDA would issue product-specific guidance: for 90% of NCE NDAs approved on or after October 1, 2017, at least two years prior to the earliest lawful ANDA filing date
- For complex products
  - there are meetings for complex products without guidance
  - FDA would strive to issue product-specific guidance for complex products as soon as scientific recommendations are available
    - Implementation note: If a guidance is not available for NDA approved after October 1, 2017 because of scientific challenges, FDA will report these scientific challenges at the annual regulatory science public meeting

Pre-ANDA Program for Complex Products: Research

- Industry Working Group
  - If Industry forms a GDUFA II regulatory science working group,
    - then upon request of the working group to the Director of the Office of Research and Standards in the Office of Generic Drugs, FDA will meet with the working group twice yearly to discuss current and emerging challenges and concerns
  - FDA will post minutes of these meetings on its website
- Reporting
  - Annually, FDA will report on its website the extent to which GDUFA regulatory science-funded projects
    - support the development of generic drug products
    - the generation of evidence needed to support efficient review and timely approval of ANDAs
    - the evaluation of generic drug equivalence
- Save the Date
  - May 24, 2018: Regulatory Science Public Meeting

Product Development Meetings

- Accelerate access to generic version of complex products by enabling potential ANDA applicants to get feedback on innovative and efficient methods to demonstrate equivalence

Pre-Submission Meetings

- Help applicants develop more complete submissions
- Promote a more efficient and effective review process
- Reduce the number of review cycles necessary to obtain ANDA approval of complex products

Mid-Review-Cycle Meetings

- If you had a pre-ANDA meeting on a complex product and use the same pre-assigned ANDA number to submit an ANDA
- After you submit your ANDA the RPM will contact you to arrange a mid-review-cycle teleconference with the FDA staff reviewing your application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