Pathways for Receiving FDA's Feedback on Formulations

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Excipients and Formulation Assessments of Complex Generic Products:
Best Practices and Lessons Learned
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Overview

- Background
- Controlled Correspondences
- Product Development Meetings

Background

- Regulations generally require that certain proposed products be qualitatively (Q1) and quantitatively (Q2) the same as the reference listed drug (RLD) with respect to certain inactive ingredients
- FDA recommends that applicants request a Q1/Q2 assessment for potential formulations prior to submitting an ANDA

Controlled Correspondence

- Purpose: a mechanism for a generic drug manufacturer or related industry to request information on a specific element of generic drug development and for the Agency's direct, brief, and timely response

Controlled Correspondence

- For products where Q1/Q2 sameness is required by the regulations
- For products where Q1/Q2 sameness is not required by the regulation, but recommended in a guidance (e.g., product-specific guidance recommends a specific bioequivalence (BE) approach)

When Submitting…

FDA recommends the controlled correspondence include the information about the RLD such as:

- Application holder
- Application number
- Proprietary name
- Active ingredient
- Strength (specify fill volume of parenteral drug products)
- Dosage Form
- Route of Administration
- Approval date
- Marketing status (i.e., whether the product is prescription, over-the-counter, or in the "Discontinued" section of the Orange Book (which includes drug products that have been withdrawn from the market))

Reminders

- If a requestor is seeking formulation assessment for multiple drug products, FDA recommends that each drug product request be submitted in a separate controlled correspondence
  - Requests for Q1/Q2 formulation assessment for drug products with different RLDs
  - Requests for Q1/Q2 formulation assessment for drug products with multiple strengths because each strength is a separate drug product
- FDA recommends that no more than three proposed Q1/Q2 formulations of a single drug product be submitted in one controlled correspondence

Controlled Correspondence

- FDA does not intend to review proposed formulations for which Q1/Q2 sameness is…
  - not required by regulation
  - not recommended as part of a BE approach in a guidance
- Formulations that are not Q1/Q2 the same as the RLD are permissible for certain products as long as the differences do not affect the safety or effectiveness of the product
  - The acceptability of such differences would be considered in the context of an ANDA review

Controlled Correspondence

- Note: The Agency is limited in the amount or type of information that FDA may disclose in response to a request for Q1/Q2 sameness assessment because formulations generally are trade secret information
- FDA does not intend to provide clarification on why a formulation is not Q1/Q2 the same as the RLD

Meetings

- Example: Product Development Meetings
  - Questions related to an ANDA development program
  - A forum for a scientific exchange on specific issues (e.g., a proposed study design, alternative approach, additional study expectations, or questions), in which FDA agreed to provide targeted advice regarding an ongoing ANDA development program

Meetings

- Example: Product Development Meetings (cont'd)
  - Development of a complex generic product for which FDA has not issued a product-specific guidance
  - An alternative equivalence approach (i.e., change in study type, such as in vitro to comparative clinical endpoint) for a complex product for which FDA has issued a product-specific guidance
  - A controlled correspondence response would not adequately address the prospective ANDA applicant's questions

Meetings

- After Product Development Meetings
  - If a prospective ANDA applicant is seeking further clarification or has new questions related to what was discussed at the meeting, FDA recommends that the applicant submit such a request, with any new information or data, in a controlled correspondence

Meetings

- If the new information, data, or questions for Agency input will not be adequately addressed in a controlled correspondence...
  - The prospective ANDA applicant can request an additional product development meeting
  - FDA will determine whether to grant the subsequent product development meeting based on the content of the meeting request and meeting package and available resources

References

- Guidance for Industry on *Controlled Correspondence Related to Generic Drug Development (December 2020)*
- Guidance for Industry on *Formal Meetings Between FDA and ANDA Applicants of Complex Products under GDUFA (October 2022, Revision 1)*


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