

Mastering Controlled Correspondences: What, When, and How

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Navigating Controlled Correspondences to
Support Generic Drug Development
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Learning objectives

- To better understand controlled correspondences (CCs) related to generic drug development through discussing
 - What: role of CCs
 - When: scope/topics to be included in CCs
 - How: common issues and general recommendations

What is a controlled correspondence

- CCs are written inquiries to the FDA for information on a specific element of generic drug development or certain post-approval submission requirements.
- CCs are triaged by the Office of Generic Drugs (OGD) to corresponding discipline within OGD or outside OGD (e.g., quality questions to the Office of Pharmaceutical Quality)

Role of CCs during Generic Development



- Specific inquiries: allowing for detailed questions regarding a particular element of generic development, like formulation, bioequivalence (BE) studies, or quality and manufacturing processes
- Early feedback: proactive engagement with FDA seeking input on critical aspects of a development program
- Improved communication: a timely and structured communication channel fosters a collaborative environment between FDA and generic industry, leading to clear expectations
- Reduced delays/assessment cycles: Addressing potential critical problems can reduce the likelihood of delays during development and ANDA assessment and facilitate preparation of ANDA submission

Examples of When CCs may be Used

- To obtain feedback on the potential acceptability of a proposed analytical methods for testing/characterizing formulations
- To seek clarification on the design of BE studies
- To discuss potential deviation and/or alternative approaches to the recommendations in product specific guidances (PSGs)
- To inquire about the interpretation of a regulatory guidance related to a specific aspect (e.g., pH adjuster guidance for non-Q1/Q2 formulations)
- To discuss the appropriateness of a proposed quality control strategy, stability testing plans, and/or manufacturing process

Common Issues of CCs

- Not enough background information and/or supportive data
- Lack of clarity
 - Questions are phrased poorly
 - Too much irrelevant information or lengthy/detailed info without specificity
- Too general
 - Questions cannot be directly addressed at pre-ANDA stage (e.g., acceptability of a specification)
 - Provide a study plan/protocol without specific questions
- Mixed questions involving multiple disciplines

General Recommendations for Preparing Good CCs



- Provide sufficient background information and/or supportive data
- Propose concise question(s)
 - Raise specific technical and/or regulatory requests (i.e., study protocols, alternative BE study design)
 - Ask questions seeking for feedback on the proposed strategy/thinking instead of open-ended questions
 - For Q1Q2 CCs, provide sufficient information demonstrating knowledge on the reference listed drug and clearly describe potential formulation differences if there are intentional formulation changes (e.g., exception excipients, and/or pH adjusters)
- If Q1Q2 formulation sameness/similarity is required per regulation or is recommended to follow a BE study design, resolve the Q1Q2 issues before proceeding with other related developmental questions.
- Separate CCs for different disciplines (e.g., BE and quality)

Advancements in CC Responses

- For Q1Q2 CCs, provide concise instruction on the essential information to allow proper assessment. When appropriate (i.e., without disclosure concerns), provide guidance on potential regulatory pathway to enable filing.
- Restructure response by indicating whether a proposal is acceptable, not acceptable or provisional.
- Recommend to submit a pre-ANDA development meeting request for further discussion when the CC contains complex questions, such as alternative BE design, which warrant further discussion across multiple disciplines.

How are CCs Used within the FDA



- Evaluate effectiveness, clarity, and relevance of guidance recommendations
 - Product specific guidance
 - pH adjuster guidance
 - Topical Q3 guidances
 - Quality focused guidances
- Implement continual improvements in regulatory practice
- Promote development of new initiatives (e.g. research efforts and/or policy)

Questions?

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