

Best Practices for Abbreviated New Drug Applications (ANDAs) in GDUFA III: A Bioequivalence Perspective

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Learning Objectives

- Explain how to engage with the Office of Bioequivalence during various stages of the ANDA lifecycle
- Provide an overview of bioequivalence communications during ANDA assessment cycles
- Review best practices

Engagement with the Office of Bioequivalence (OB) in GDUFA III



Engaging with OB Prior to ANDA Submission

Meetings	<ul style="list-style-type: none">• Product Development Meeting• Pre-Submission Meeting• Pre-Submission Product-Specific Guidance (PSG) Teleconference• Pre-Submission PSG Meeting
Written Communication	<ul style="list-style-type: none">• Controlled Correspondence<ul style="list-style-type: none">▪ Inactive Ingredients▪ Specific generic drug development questions related to bioequivalence▪ Risk Evaluation and Mitigation Strategies (REMS) with Elements to Assure Safe Use (ETASU) Protocols▪ Feedback after Pre-Submission PSG Teleconference

Engaging with OB During ANDA Assessment

Meetings	<ul style="list-style-type: none"> • Post-Submission PSG Teleconference • Post-Submission PSG Meeting • Mid-Cycle Review Meeting • Enhanced Mid-Cycle Review Meeting
Written Communication	<ul style="list-style-type: none"> • Controlled Correspondence • General Correspondence

Engaging with OB Post-Complete Response Letter (CRL)

Meetings	<ul style="list-style-type: none"> • Post-CRL Teleconference (Clarification) • Post-CRL Scientific Meeting • Post-Submission PSG Teleconference • Post-Submission PSG Meeting
Written Communication	<ul style="list-style-type: none"> • Controlled Correspondence

Engaging with OB Post Approval

Written Communication

- Controlled Correspondence

Overview of Bioequivalence Communications During ANDA Assessment Cycles in GDUFA III



GDUFA III ANDA Assessment Program Enhancements

- Goals
 - Improve predictability and transparency
 - Promote efficiency and effectiveness of the review process
 - Minimize the number of assessment cycles needed for approval
 - Increase the overall rate of approval
 - Facilitate greater access to generic drug products

Information Requests (IRs)

- Sent during assessment cycle to request further information/clarification needed to complete discipline assessment
- Does not stop assessment clock
- Deficiencies identified as major or minor
- Generally includes requested response due date
- Typically communicated by e-mail

Discipline Review Letters (DRLs)

- Convey preliminary thoughts on possible deficiencies at conclusion of discipline assessment
- First assessment cycle DRL issued by mid-point and includes requested response due date
- Deficiencies identified as major and minor
 - Responses to minor DRLs received by due date reviewed within original goal date
 - Responses to major deficiencies or minor deficiencies requiring comparable FDA assessment resources as major deficiencies classified as major amendments and goal date extended

IRs and DRLs (cont.)

- IRs and DRLs issued after first assessment cycle mid-point
 - When minor deficiencies can be resolved using an IR or DRL and ANDA may be approved or tentatively approved in current assessment cycle
 - Will identify major and minor deficiencies and may assign due date
 - Goal date may be extended by 90 days from date of response
 - DRLs without a response due date may signify a forthcoming CRL

Best Practices



Controlled Correspondence

- Submit through the CDER Direct NextGen Collaboration Portal and not to individuals at FDA
- Ensure inquiries are specific and contain sufficient detail
- Limit requests to one discipline
- Do not submit same question(s) utilizing multiple submission routes

Controlled Correspondence

- Inactive Ingredient Requests
 - Submit no more than three inactive ingredients and no more than three proposed levels for a drug product
 - Only submit inactive ingredients to be evaluated and their proposed levels
 - Identify the reference listed drug (RLD), including specific drug product strength(s)

Cover Letter

- Outline of disciplines impacted by submission
- Information on previous communications with the Agency
- Controlled Correspondence, if inquiry is related to an ANDA
- ANDA submissions, indicate:
 - Active Pharmaceutical Ingredient (API) source changes
 - Submission of new bioequivalence studies conducted at a new contract research organization

Responses to IRs/DRLs

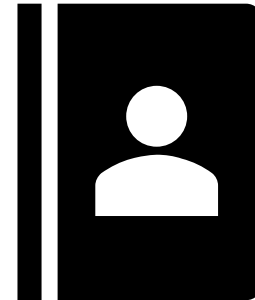
- Respond to IR/DRLs completely and by response due date!
 - Partial responses will **not** be accepted
 - If a complete response is not provided by due date, deficiencies may be included in CRL
 - Be clear and concise and only respond with requested information

IR/DRL Extension Requests

- Submit an extension request as soon as possible if unable to respond by due date
 - Point of contact for Bioequivalence IRs and DRLs is the OB Project Manager (PM) listed on the letter
- Extension requests will be reviewed on a case-by-case basis

FDA Contacts

- General ANDA questions: OGD RPM
- Bioequivalence IR and DRL questions: OB PM
- Quality related questions: OPQ RBPM



Challenge Question #1

In GDUFA III, during the ANDA assessment cycle, a controlled correspondence may be submitted in which of the following situations?

- A. After a PSG Teleconference
- B. When seeking a Covered Product Authorization
- C. For any clarification questions
- D. A and B only
- E. All of the above

Challenge Question #2

Which of the following is true about first assessment cycle DRLs in GDUFA III?

- A. Will be issued by the assessment cycle mid-point
- B. Deficiencies will be classified as major or minor
- C. A response due date will be included
- D. Responses to major DRLs will extend the goal date
- E. All of the above

Resources

- [GDUFA III Reauthorization](#)
- [GDUFA III Commitment Letter](#)
- [Guidance for Industry: Controlled Correspondence Related to Generic Drug Development](#)
- [Guidance for Industry: Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA](#)
- [Guidance for Industry: Product-Specific Guidance Meetings Between FDA and ANDA Applicants Under GDUFA](#)

Resources

- [Guidance for Industry: Post-Complete Response Letter Clarification Teleconferences Between FDA and ANDA Applicants Under GDUFA](#)
- [Guidance for Industry: Information Requests and Discipline Review Letters Under GDUFA](#)
- [MAPP 5220.5 Rev. 2: Issuance of Information Requests and/or Discipline Review Letters for ANDAs](#)

Conclusion

- Be familiar with expanded definitions of controlled correspondence, new meeting types, and communication enhancements in GDUFA III
- Follow best practices discussed to reduce the number of bioequivalence assessment cycles
- Reach out to the OB Project Manager for questions related to Bioequivalence IRs and DRLs



Thank You

