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	• Product Development Meeting • Pre-Submission Meeting • Pre-Submission Product-Specific Guidance (PSG) Teleconference • Pre-Submission PSG Meeting
Written Communication	• Controlled Correspondence ▪ 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	• Post-Submission PSG Teleconference • Post-Submission PSG Meeting • Mid-Cycle Review Meeting • Enhanced Mid-Cycle Review Meeting
Written Communication	• Controlled Correspondence • General Correspondence

Engaging with OB Post-Complete Response Letter (CRL)

Meetings	• Post-CRL Teleconference (Clarification) • Post-CRL Scientific Meeting • Post-Submission PSG Teleconference • Post-Submission PSG Meeting
Written Communication	• 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

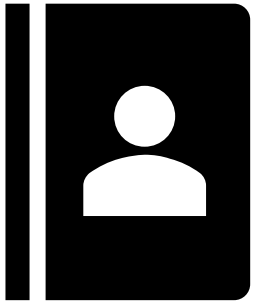
- Respond to IR/DRLs completely and by response due date!
  - Partial responses will **not** be accepted
  - If a complete response is not provided by due date, deficiencies may be included in CRL
  - Be clear and concise and only respond with requested information

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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