

Draft Guidance for Industry:
ANDA Submissions –
Amendments to Abbreviated New Drug
Applications Under GDUFA



Guidance Purpose and Goals

- Explains how the review goals established as part of the Generic Drug User Fee Amendments Reauthorization of 2017 (GDUFA II) apply to amendments to ANDAs and PASs
- Explains how submission of amendments may affect an application's review goal date
- Describes the classification and categories of amendments



Amendments Under GDUFA I

- Amendments were classified into a complex Tier system based on:
 - whether the amendment was solicited or unsolicited;
 - whether the amendment was major or minor;
 - the number of amendments submitted; and
 - whether an inspection was necessary to support the information contained in the amendment



Amendments Under GDUFA II

- Amendments under GDUFA II are no longer subject to a Tier system and review goals are simplified
- GDUFA II amendments:
 - Designated as standard or priority,
 - Classified as major or minor, and
 - Receive a goal date based on the factors identified in the Commitment Letter and Section IV of the guidance



Amendments Under GDUFA II

- Each and every submission to the received application is an amendment
 - Review goals do not apply to submissions pending filing review
- Each submission will be classified based on the content submitted and will be issued a goal date consistent with that classification

Categories of Amendments

- Major
 - New batches
 - New bioequivalence studies
 - New analytical methods
 - See Appendix A
- Minor
 - Minor deficiencies in the drug master file
 - Incomplete dissolution data
 - Labeling deficiencies
- Unsolicited
 - Information not requested by FDA

Review Goals - ANDAs

Amendment Type	Performance Goal
Standard major	90% reviewed within 8 months of submission date if preapproval inspection (PAI) is not required
	90% reviewed within 10 months of submission date if PAI is required
Priority major	90% reviewed within 6 months of submission date if PAI is not required
	90% reviewed within 8 months of submission date if: <ol style="list-style-type: none"> (1) PAI is required; (2) applicant submits a complete and accurate PFC no later than 60 days prior to the date of the amendment submission; and (3) the PFC remains unchanged at the time of amendment submission
	90% reviewed within 10 months of submission date if: <ol style="list-style-type: none"> (1) PAI is required and (2) applicant fails to submit a complete and accurate PFC no later than 60 days prior to the date of the amendment submission; or (3) information in a complete and accurate submitted PFC changes
Standard or Priority minor	90% reviewed within 3 months of the submission date

Review Goals - PASs

Amendment Type	Performance Goal
Standard major	90% reviewed within 6 months of submission date if PAI is not required
	90% reviewed within 10 months of submission date if PAI is required
Priority major	90% reviewed within 4 months of submission date if PAI is not required
	90% reviewed within 8 months of submission date if: <ol style="list-style-type: none"> (1) PAI is required; (2) applicant submits a complete and accurate PFC no later than 60 days prior to the date of the amendment submission; and (3) the PFC remains unchanged at the time of amendment submission
	90% reviewed within 10 months of submission date if: <ol style="list-style-type: none"> (1) PAI is required and (2) applicant fails to submit a complete and accurate PFC no later than 60 days prior to the date of the amendment submission; or (3) information in a complete and accurate submitted PFC changes
Standard or Priority minor	90% reviewed within 3 months of the submission date

Review Goals

- Review unsolicited amendments to ANDAs and PASs submitted *during* the review cycle by the later of:
 - (1) the goal date for the original submission/solicited amendment, or
 - (2) the goal date assigned in accordance with the goals for standard and priority review ANDAs and PASs
- Review unsolicited amendments to ANDAs and PASs submitted *between* review cycles by the later of
 - (1) the goal date for the subsequent solicited amendments, or
 - (2) the goal date assigned in accordance with the goals for standard or priority ANDAs and PASs

Amendments pre-GDUFA II

- Any submission that did not have a GDUFA I goal date or Target Action Date (TAD), will receive a GDUFA II Date
- FDA will continue to review amendments that have a GDUFA I review goal date and act on those submissions by the GDUFA I goal date
- FDA will review and act on 90% of amendments with TADs by the goal date (converted to a GDUFA II goal date)



Application of Review Goals

- Changes to classification or review goal
 - FDA may change classification of a response to a Complete Response Letter (CRL) or its initial classification of an unsolicited amendment based on the content of the amendment
 - If FDA determines that a PAI is required during the review of an unsolicited or solicited minor amendment, FDA will classify the submission as a major amendment and set a review goal of 10 months from the date of submission



Application of Review Goals

- Changes to classification or review goal (cont'd)
 - If an applicant does not submit a response to an Information Request (IR) or Discipline Review Letter (DRL) by the date requested by FDA, FDA may reissue the IR or DRL as a deficiency in a CRL
 - If an applicant submits a timely response to an IR or DRL, but the response contains information requiring more extensive review than is typically required for such deficiencies, the response will be classified as a minor or major and the goal date adjusted accordingly



Application of Review Goals

- Deferred amendments
 - FDA will generally accept an unsolicited amendment submitted during the review cycle and adjust the goal date for the application
 - FDA may defer review of an unsolicited amendment if
 - the reviews are close to completion and the submitted amendment contains a significant amount of new information to be reviewed
 - the amendment is submitted after the relevant reviews have been completed and an IR, DRL, or CRL is being prepared

Application of Review Goals

- Amendments submitted before and after 10/1/17
 - If an applicant submits an amendment on or after 10/1/17, to an amendment under review that is subject to a TAD or GDUFA I review goal, FDA will review both amendments by either the TAD or GDUFA I review goal or the GDUFA II review goal, whichever is longer

Application of Review Goals

- Amendments to tentatively approved ANDAs
 - Requests for final approval
 - A request for final approval with no new data, information, or other changes to the ANDA generally requires 90 days for FDA review
 - A request for final approval with substantive changes to the ANDA or changes in the status of the manufacturing and/or testing facilities' compliance with current good manufacturing practices, or the addition of new facilities, will be classified as a major or minor amendment and will be assigned the corresponding review goal date

Application of Review Goals

- Amendments to tentatively approved ANDAs
 - Amendments other than requests for final approval
 - Amendments between the tentative approval (TA) and the request final approval will be classified as unsolicited but may not be reviewed on submission
 - FDA will not delay review of amendments submitted to President's Emergency Plan for Aids Relief (PEPFAR) ANDAs that have received TA
 - FDA will review upon submission and set a goal date consistent with the criteria outlined in the guidance

Application of Review Goals

- Amendments submitted in response to changes in the DMF
 - Changes made to a DMF referenced in an ANDA that may impact the safety, efficacy, quality, or substitutability of the drug product may be considered unsolicited amendments to the ANDA, and may extend existing review goals or create new review goals

Submission and Receipt of Amendments



Include with the amendment, as applicable:

A statement indicating whether the amendment is unsolicited or in response to a request from FDA

The discipline from which the IR/DRL was issued or the disciplines from which the CRL was issued

The amendment classification (major or minor) as identified by FDA

If unsolicited, the amendment classification proposed by the applicant

A statement indicating that the application should be classified as priority (including justification)

A statement indicating that the applicant is requesting priority review for the amendment (including justification)

A statement indicating if and when a PFC was submitted

A statement indicating if the amendment is addressing a change in the DMF

A statement indicating whether the amendment contains any manufacturing or facilities changes

Submission and Receipt of Amendments



- The regulatory project manager will issue an acknowledgment letter to confirm submission of the amendment
- The acknowledgment letter will not state whether a PAI is required, but will state two possible goal dates: the goal date *with* an inspection and the goal date *without* an inspection

Requests for Reconsideration of Major Amendment Classification Status

- Applicants may request reconsideration of major amendment classification via teleconference
- FDA will schedule and conduct the teleconference and decide 90% of such requests within 30 calendar days of receipt of the request
- Requests should be submitted to the ANDA, with a copy to the appropriate signatory authority and ANDAREconsideration@fda.hhs.gov



Please contact CDERSBIA@fda.hhs.gov with any questions. Thank you.