
POLICY AND PROCEDURES

**OFFICE OF GENERIC DRUGS AND OFFICE OF PHARMACEUTICAL
QUALITY**

Good Abbreviated New Drug Application Assessment Practices

Table of Contents

PURPOSE.....1
BACKGROUND1
POLICY4
RESPONSIBILITIES.....5
PROCEDURES5
REFERENCES.....10
DEFINITIONS10
EFFECTIVE DATE.....11
CHANGE CONTROL TABLE.....11

PURPOSE

This Manual of Policies and Procedures (MAPP) establishes good abbreviated new drug application (ANDA) assessment practices for the Office of Generic Drugs (OGD) and the Office of Pharmaceutical Quality (OPQ) to increase their operational efficiency and effectiveness, with a goal of decreasing the number of review cycles to approve ANDAs that meet the requirements for approval.

BACKGROUND

Under the Generic Drug User Fee Amendments of 2012 (GDUFA I),¹ the Food and Drug Administration (FDA) executed a deep, foundational restructuring of the ANDA review program. As part of this restructuring, FDA adopted performance goals for the review of ANDAs; overhauled the generic drug program’s business processes; developed and implemented an integrated ANDA review information platform; reorganized OGD; established OPQ to, among other things, integrate the ANDA quality assessment; and hired and trained over 1,000 employees. As a direct result of this restructuring, FDA’s efficiency and output from ANDA review improved, including issuance of complete response letters as well as increased ANDA approvals.

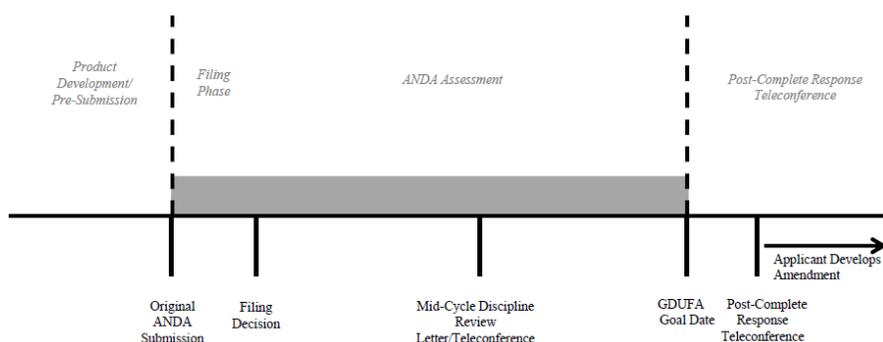
¹ Food and Drug Administration Safety and Innovation Act (Public Law 112-144).

Still, prior to October 1, 2017, about half of all ANDAs with GDUFA I goal dates required three or more review cycles to reach approval or tentative approval. Multiple cycles are highly inefficient, require significant resources from applicants and FDA, and delay timely consumer access to generic medicines.

Accordingly, after receiving public input, FDA and industry negotiated a revised agreement, the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Commitment Letter),² and the generic drug user fee program was reauthorized through the Generic Drug User Fee Amendments of 2017 (GDUFA II)³ on August 18, 2017. The GDUFA II ANDA review program instituted substantial program enhancements at every major stage of the ANDA development and review timeline, including: product development, pre-submission, filing, mid-review, late review, post-complete response letter, and approval/tentative approval. These program enhancements should foster the development of high-quality submissions, ensure the timely resolution of filing reconsideration requests, promote the correction of deficiencies within the current review cycle, and support the development of high-quality re-submissions. As a result, the number of review cycles to reach approval is expected to decrease.

Figure 1 below displays, horizontally, a timeline that illustrates the historic process for developing and reviewing ANDAs. The shaded portion of the figure illustrates the time spent by the OGD and OPQ technical disciplines (i.e., bioequivalence, labeling, and quality) in assessing whether ANDAs met the requirements for regulatory approval.

Figure 1. ANDA Timeline

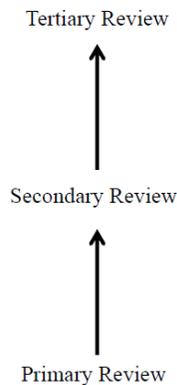


² This agreement is available at <https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf>.

³ Food and Drug Administration Reauthorization Act of 2017 (Public Law 115-52).

The customary review process of recent years is displayed vertically in Figure 2 below, which illustrates that a primary review was often followed by a secondary review, which was sometimes followed by a further (or tertiary) review.

Figure 2. Technical Review Process of Recent Years



Over the past several decades, ANDA review customs have evolved, and the quantity of documentation of FDA’s ANDA review has increased. During this time, supervisor expectations concerning review documentation occasionally varied within and across disciplines. For instance, reviewers sometimes evaluated ANDAs beyond what was necessary to ensure that the ANDA met the regulatory requirements for approval, worked to remediate and re-assemble poorly organized ANDAs, or generated elaborate work papers.

OGD and OPQ’s consistent and targeted focus should continue to be on evaluating whether ANDAs meet the regulatory requirements for approval. To reinforce the policy and procedural changes set forth in this MAPP, going forward, OGD and OPQ will use the term *assessment* in place of *review*. *Assessment* means the process of both evaluating and analyzing submitted data and information to determine whether the application meets the requirements for approval and documenting that determination.

Although nothing in this MAPP alters the regulatory requirements for ANDA approval, this MAPP makes three significant changes to FDA’s ANDA assessment practices.

This MAPP:

- Establishes that assessment teams should, when available, use templates and assessment tools provided by the sub-disciplines that focus the primary assessment of quality, bioequivalence, or labeling data or information on the

critical attributes of the application. These critical attributes templates and assessment tools will help guide assessors to convey:

- Their determination of whether the application meets the requirements for approval
- Their message to applicants, when applicable, explaining the deficiency, why a major or minor amendment is necessary to respond to that deficiency (e.g., by referencing guidance documents), and what missing or additional information is needed to support an approval decision
- Clarifies the roles and responsibilities of primary assessors, secondary assessors, and division directors (who, under this MAPP, will no longer perform the role of a typical tertiary reviewer). This clarification will reduce duplicative and unnecessary work, which will increase FDA's efficiency and effectiveness.
- Establishes that OGD and OPQ will clearly communicate to applicants what deficiencies must be corrected for their ANDAs to be approved. This communication will enable applicants to develop high-quality re-submissions and to reduce the number of subsequent cycles to approval.

Collectively, these changes are expected to expand access to generic medicines and enable OGD's and OPQ's highly trained experts to focus more of their attention on novel or challenging scientific and policy issues associated with the development and assessment of generic drug products.

This MAPP was developed by OGD and OPQ in close collaboration with both offices' senior technical discipline leadership and staff.

FDA is publishing this MAPP concurrently with the draft guidance for industry *Good Abbreviated New Drug Application Submission Practices*.⁴ This guidance highlights common, recurring deficiencies that may delay approval of an ANDA and makes recommendations to applicants on how to avoid these deficiencies. The guidance and this MAPP will build upon the success of the generic drug user fee program to help reduce the number of review cycles for an ANDA to attain approval.

POLICY

- The purpose of the ANDA assessment is to determine whether an ANDA meets the requirements for regulatory approval. Regulatory requirements for approval

⁴ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA Drugs guidance web page at <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

exist in relevant statutory provisions and regulations but may also be addressed in guidance documents.

- Critical attributes templates and assessment tools, developed by the technical (sub)disciplines, structure the primary assessment and ensure its focus is on whether the application meets the regulatory requirements for approval. Use of these templates and assessment tools should increase the efficiency of the primary assessment by focusing the assessment and eliminating unnecessary documentation, improving assessment consistency within a (sub)discipline, and improving the ease of review by secondary assessors.
 - Primary assessors, secondary assessors, and division directors have distinct, but closely related and complementary roles and responsibilities.
 - OGD and OPQ will clearly explain to applicants what deficiencies they must correct to obtain ANDA approval.
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RESPONSIBILITIES

- Primary assessors recommend whether ANDAs meet the regulatory requirements for approval.
 - Secondary assessors validate primary assessments and communications as being consistent with current policies and procedures.
 - Absent unique circumstances, division directors do not assess ANDAs. Instead, division directors focus on managing practices within their divisions and are available for consultation by assessors.
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PROCEDURES

1. Original ANDAs

A. *Primary Assessors*

- Primary assessments are to evaluate and recommend whether an ANDA meets the regulatory requirements for approval.
 - Primary assessors use the technical (sub)discipline's critical attributes templates and assessment tools, when available, to assess whether the ANDA meets the regulatory approval requirements. These templates and assessment tools may constitute the primary assessment documentation or may be incorporated within an assessment document.
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- When the primary assessor needs to incorporate information from the ANDA into the assessment document template, the best approach is to document by reference, either by hyperlink⁵ or by section and page number. For example, primary assessors do not need to provide a lengthy, detailed summary of a drug product method validation report in their assessment. Instead, primary assessors can evaluate the report, reference the appropriate section of the ANDA that contains the report (e.g., section 3.2.P.5.3), cite the page number of the appropriate section, and document their evaluation of the submitted data. If the primary assessor determines it is not the best approach to document by reference, the primary assessor should briefly and concisely summarize key information in the ANDA (e.g., tables and bullet points may be used to convey summarized information) and reference the section of the ANDA where this information can be found.
- Primary assessors keep copying and pasting to a minimum. Primary assessors should not copy and paste ANDA content into the assessment template or document unless it is essential or more efficient to do so (e.g., in a specification table).
- Primary assessors do not rewrite, reorganize, reassemble, or remediate the ANDA. As described in FDA's draft guidance for industry *Good ANDA Submission Practices*, it is the ANDA applicant's responsibility to submit a high-quality and complete ANDA.
- Primary assessors focus on relevant information (i.e., information that is necessary to ensure that the ANDA meets the regulatory requirements for approval) in their specific discipline. Information that is scientifically or academically interesting but is not needed to make a regulatory decision is not relevant. In other words, primary assessors should focus on issues in their specific discipline that are *need to know* and not *nice to know*.
- The extent of the assessment and related documentation should be proportionate to (1) the novelty, complexity, and level of potential risk to quality posed by product attributes or process characteristics and (2) whether the decision will establish a precedent or new policy. If primary assessors have questions about the appropriate extent of their assessment and documentation, they consult their supervisor.

⁵ The primary assessor should document by hyperlink to the ANDA in GlobalSubmit only if the hyperlinks are maintained when the document is archived in PDF format.

- If the ANDA meets the regulatory requirements for approval, the primary assessor recommends approval.
- If the ANDA does not meet the regulatory requirements for approval, the primary assessor's communication to the applicant references the application and explains what deficiencies must be corrected for the ANDA to be approvable. The primary assessor:
 - Ensures that the discipline review letter or complete response letter refers to a specific location within the ANDA to provide a point of reference for the deficiency
 - Identifies any omitted information or explains the problem with the information submitted
 - Explains the actions necessary for the applicant to resolve the deficiency (including alternative approaches, if applicable)
 - Explains why the requested information or revision is needed (i.e., the communication should clearly reference the ANDA and explain what deficiencies must be corrected for the ANDA to be approvable and why a major or minor amendment is necessary to respond to each deficiency (e.g., by referencing guidance documents))
- If the communication is a discipline review letter, the primary assessor follows discipline procedures regarding next steps. If the communication is a complete response letter, the primary assessor forwards the ANDA to the secondary assessor.

B. Secondary Assessors

- Secondary assessments provide scientific and regulatory oversight of primary assessments, specifically to ensure the quality of the technical assessment, the quality of the communication to the applicant, and consistency with similar assessments and current policies and procedures.
- The secondary assessor should *assess* the assessment, not *conduct* the assessment.
- The extent of the secondary assessment reflects the experience and expertise of the primary assessor; the novelty, complexity, and level of potential risk to quality posed by product attributes or process characteristics; and whether the decision would establish a precedent

and/or change in policy. For example, when the primary assessor is a new employee, the secondary assessment may warrant more oversight or time for discussion about key issues, while only occasional spot checks may be needed for experienced primary assessors.

- The secondary assessor does not redo the primary assessment (e.g., routinely *fact check* deficiencies, routinely *dive down* into the ANDA or assessment, or otherwise search for errors or ambiguities in FDA's assessment and response to the applicant). If the secondary assessor identifies shortcomings in the primary assessment, the primary assessor should receive coaching or additional training, as appropriate, concerning assessment expectations.
- Secondary assessors confirm, as appropriate per discipline procedures, that the communication to the applicant references the application and explains what deficiencies must be corrected for the ANDA to be approvable. The secondary assessor ensures, as appropriate per discipline procedures, that primary assessors:
 - Included in discipline review letters and complete response letters a reference to a specific location within the ANDA to provide a point of reference for the deficiency
 - Identified any omitted information or explained the problem with information submitted
 - Explained the actions necessary to resolve the deficiency (including alternative approaches, if applicable)
 - Explained why the requested information or revision is needed (i.e., the communication should clearly reference the ANDA and explain what deficiencies must be corrected for the ANDA to be approvable and why a major or minor amendment is necessary to respond to each deficiency (e.g., by referencing guidance documents))
- After the secondary assessor concurs with the primary assessment, he or she forwards the ANDA for the next steps leading to a regulatory action.

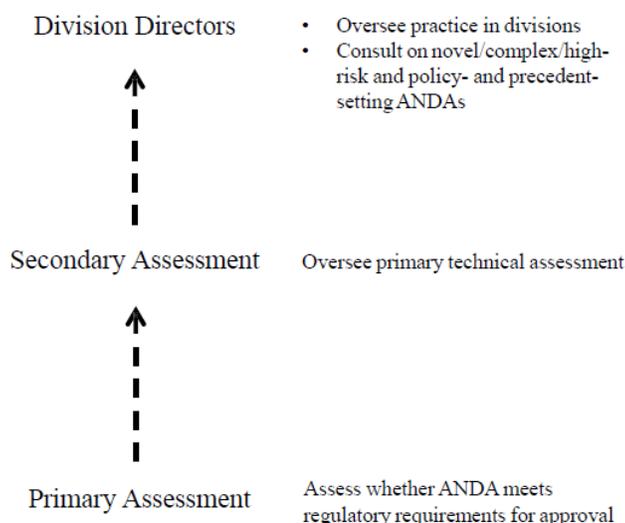
C. *Division Directors*

- The division director ensures that the division is adhering to good ANDA assessment practices as outlined in this MAPP.

- The division director ensures consistency across teams and within his or her specific (sub)discipline.
- Absent unique circumstances, the division director does not redo primary or secondary assessments or *dive down* into the ANDA or assessment.
- The division director proactively raises emerging issues and serves as a resource to assessors for consultation on novel, complex, or high-risk products and policy- and precedent-setting decisions.⁶ If the division director identifies an emerging policy issue, he or she should notify the Office of Generic Drug Policy or the Office of Policy for Pharmaceutical Quality, as appropriate.

Figure 3 depicts, vertically, the process for good ANDA assessment practices.

Figure 3. Good ANDA Assessment Practices



2. Amendments

- Primary and secondary assessors focus their assessment on issues within the narrow scope of the amendment. They should not revisit resolved issues from the original ANDA submission. In the assessment of an amendment, primary and secondary assessors also should not address new issues outside the scope of or unrelated to the issue raised in the prior communication for which the amendment was submitted. This includes situations where the assessor was

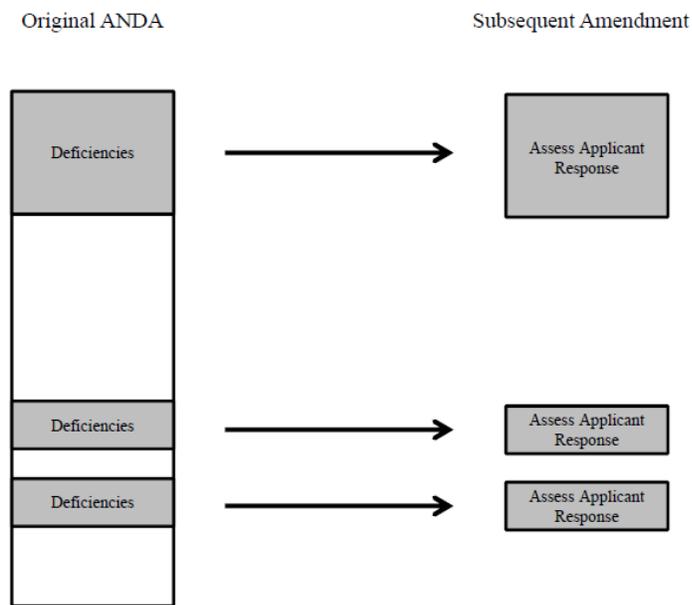
⁶ In some cases, such as for unusually complex products or for precedent-setting decisions, the senior scientific advisor (or equivalent) may be consulted instead of, or in addition to, the division director.

reassigned the amendment for workload management reasons and he or she did not conduct the original assessment.

- If the amendment contains information not requested in or related to a discipline review letter or complete response letter, the primary assessor contacts the appropriate project manager.

Figure 4 illustrates that primary and secondary assessors focus their assessment on issues within the narrow scope of the amendment.

Figure 4. Scope of Amendment Assessment



REFERENCES

- CDER MAPP 4151.8 *Equal Voice: Discipline and Organizational Component Collaboration in Scientific and/or Regulatory Decisions*
- Draft Guidance for Industry, *Good Abbreviated New Drug Application Submission Practices*

DEFINITIONS

- **Assessment:** The process of both evaluating and analyzing submitted data and information to determine whether the application meets the requirements for approval and documenting that determination.

- **Primary assessment:** The main technical and regulatory evaluation of submitted data and information to determine whether the application meets the regulatory requirements for approval.
- **Secondary assessment:** A higher level evaluation of the primary assessment to ensure completeness and consistency with current policies and procedures.
- **Critical attributes template:** A discipline-specific template used to guide the primary assessor’s evaluation of submitted data and information, identify the regulatory requirements for approval, and capture the primary assessor’s recommendation.
- **Discipline review letter:** A letter used to convey preliminary thoughts on possible deficiencies found by a discipline reviewer and/or review team for its portion of the pending application at the conclusion of the discipline review.
- **Complete response letter:** A written communication to an applicant from FDA usually describing all of the deficiencies that the Agency has identified in a new drug application or ANDA that must be satisfactorily addressed before it can be approved.

EFFECTIVE DATE

This MAPP is effective upon date of publication and applies to all submissions, including those pending with FDA as of that date, unless otherwise noted.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
1/3/18	Initial	N/A