POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

Good Abbreviated New Drug Application Assessment Practices

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PURPOSE

This Manual of Policies and Procedures (MAPP) revises the 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 needed 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) implemented a restructuring of the ANDA assessment 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).

The generic drug user fee program was reauthorized through the Generic Drug User Fee Amendments of 2017 (GDUFA II)[2] on August 18, 2017. As outlined in the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2018-2022 (GDUFA II Commitment Letter),[3] 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, with the goal of reducing the number of assessment cycles necessary for approval.

Most recently, the generic drug user fee program was reauthorized as part of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023.[4] As described in the GDUFA Reauthorization Performance Goals and Program Enhancements Fiscal Years 2023-2027 (GDUFA III commitment letter) applicable to this latest reauthorization,[5] FDA has agreed to performance goals and program enhancements regarding aspects of the generic drug assessment program that build on previous authorizations of GDUFA. New enhancements to the program are designed to maximize the efficiency and utility of each assessment cycle, with the intent of continuing to reduce the number of assessment cycles for ANDAs and facilitating timely access to generic medicines.

ANDAs typically undergo primary and secondary assessment by the OGD and OPQ technical disciplines (i.e., bioequivalence, labeling, and quality) to determine whether they meet the requirements for regulatory approval. OGD and OPQ's consistent and targeted focus should continue to be on evaluating and analyzing submitted data and information to determine whether the application meets the requirements for approval and documenting that determination. To reinforce the policy and procedural changes set forth in this MAPP, OGD and OPQ will continue to use the term *assessment* in place of *review*. See Definitions below.

Although nothing in the previous version of this MAPP altered the regulatory requirements for ANDA approval, it made three significant changes to FDA's ANDA assessment practices.

Those changes were to:

- Establish that assessment teams should, when available, use templates and assessment tools provided by the disciplines that focus the primary assessment of

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[2] Food and Drug Administration Reauthorization Act of 2017 (Public Law 115-52).
[3] This agreement is available at https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf.
[4] See Division F, Title III of the Continuing Appropriations and Ukraine Supplemental Appropriations Act, 2023 (Public Law 117-180).
[5] The GDUFA III commitment letter is available at https://www.fda.gov/media/153631/download.

bioequivalence, quality,[6] or labeling data or information on the critical attributes of the application. These critical attributes templates and assessment tools 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

- Clarify the roles and responsibilities of primary assessors, secondary assessors, and division directors (who, under this MAPP, no longer perform the role of a typical tertiary assessor). This clarification is intended to reduce duplicative and unnecessary work to increase FDA's efficiency and effectiveness.

- Establish that OGD and OPQ will clearly communicate to applicants what deficiencies must be corrected for their ANDAs to be approved. This communication is intended to enable applicants to develop high-quality re-submissions and to reduce the number of subsequent cycles for approval.

Collectively, these changes were intended to expand access to generic medicines and enable OGD and OPQ 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.

FDA published the previous version of this MAPP concurrently with the guidance for industry *Good Abbreviated New Drug Application Submission Practices*.[7] 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 build upon the success of the generic drug user fee program to help reduce the number of assessment cycles for an ANDA to attain approval.

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

[6] FDA takes a risk-and science-based approach to product quality assessment by: 1) encouraging implementation of risk-based approaches that focus Agency attention on critical areas and 2) ensuring that assessment policies are based on advanced pharmaceutical science.

[7] 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.

POLICY

- The ANDA assessment determines whether an ANDA meets the requirements for approval. Requirements for approval[8] are primarily specified in relevant statutory provisions and regulations, while guidance documents may provide clarity on the existing requirements or recommendations on how to meet these requirements.

- Critical attributes templates and assessment tools developed by the technical disciplines structure the primary assessment, eliminate unnecessary documentation, and focus the assessment on whether the application meets the regulatory requirements for approval. Use of these templates and assessment tools helps to increase the efficiency and consistency of the primary assessment within a discipline and improves the ease of the secondary assessment.

- Primary assessors, secondary assessors, branch chiefs (OPQ) and division directors (supervisors) have distinct and complementary roles and responsibilities.

- OGD and OPQ will clearly explain to applicants the deficiencies that must be addressed to obtain ANDA approval.

RESPONSIBILITIES

- Primary assessors assess the ANDA, draft communications to the ANDA applicant, recommend whether the ANDA meets the regulatory requirements for approval and document the assessment.

- Secondary assessors validate primary assessments and communications as being consistent with current policies and procedures.

- Absent unique circumstances, supervisors do not assess ANDAs. Instead, supervisors focus on managing practices and assessment consistency within the branch or division and are available for consultation by assessors.

[8] Note that filing reviews for ANDAs are covered by CDER MAPP 5200.14, *Filing Review of Abbreviated New Drug Applications,* available at https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-manual-policies-procedures-mapp.

PROCEDURES

1. Original ANDAs

A. Primary Assessors

- Focus on information that is necessary to ensure that the ANDA meets the regulatory requirements for approval for their specific discipline. Information that is not needed to make a regulatory decision in assessing the ANDA is not relevant.

- Use the technical discipline's critical attributes templates and assessment tools, when available, to assess whether the ANDA meets the regulatory requirements for approval. These templates and assessment tools may constitute the primary assessment documentation or may be incorporated within an assessment document.

- Reference in the assessment the location of the information under assessment (e.g., URL, section, and page number), evaluate the information, and document their assessment and conclusion. When necessary, may use summary tables and bullet points to convey relevant information or findings.

- Assess the submission and related documentation 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 could establish a precedent or new policy.

  If primary assessors have questions about the appropriate extent of their assessment and documentation, they should consult the secondary assessor or the supervisor.

- Refrain from copying and pasting ANDA content into the assessment template or document unless it is essential or more efficient to do so. Rather, as appropriate, primary assessors should briefly summarize the information or reference the information location.

- Make an initial determination as to whether any potential consults will be necessary and whether there are complex issues that require prioritization or the involvement of multiple disciplines.

- When deficiencies, information gaps or discrepancies are identified during the assessment cycle, draft information requests or deficiencies to be conveyed to the applicant in a mid-cycle letter.

- Will not attempt to rewrite, reorganize, or reassemble the ANDA as it is the ANDA applicant's responsibility to submit a high-quality and complete ANDA in the appropriate submission format as described in FDA's guidance for industry *Good ANDA Submission Practices*.[9]

- Recommend approval if the ANDA meets the regulatory requirements for approval upon completion of the assessment (of the original ANDA submission and amendments containing responses to any information requests/deficiency letters).

- If the ANDA application (including any amendments containing responses to information requests and deficiency letters) does not meet the regulatory requirements for approval, draft the outstanding deficiencies that must be corrected for the ANDA to be approvable.[10]

- If the communication is a discipline review letter, follow discipline procedures regarding next steps for issuing the letter. If the communication is a complete response letter, notify the secondary assessor.

B. *Secondary Assessors*

- 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 extent of the secondary assessment should be calibrated as appropriate considering the experience, knowledge, expertise, and quality of the work product of the primary assessor; the novelty, complexity, and level of potential risk to product quality or product performance; 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.

- Will not redo the primary assessment. If the secondary assessor identifies shortcomings in the primary assessment, the primary assessor should receive coaching or additional training, as appropriate.

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[9] See also FDA guidance for industry "*Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*" (February 2020, Rev. 7).

[10] For quality-related deficiencies, see MAPP 5016.8, *Communication Guidelines for Quality-Related Information Requests and Deficiencies*.

- 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. Ensure, 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 regulations, compendia, MAPPs, and guidance documents))
- After determining concurrence with the primary assessment, moves the ANDA to the next step culminating in a regulatory action.

C. Branch Chiefs

- Ensure that the ANDA assessments within the branch are consistent and adhere to practices and policies outlined in applicable regulations, guidances, MAPPs, SOPs, and training documents.
- Do not perform tertiary assessments unless there are unique circumstances. Do not redo primary or secondary assessments.
- Serve as a resource for assessors for consultation on novel, complex, or high-risk products and policy- and precedent-setting decisions.[11] If the branch chief identifies an emerging policy issue, they should notify the division director and management, as necessary.

D. Division Director

[11] 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.

- Ensures that the assessments within the division are completed in accordance with practices and policies outlined in applicable regulations, guidances, MAPPs, SOPs, and training documents.

- Serves as a resource for assessors for consultation on novel, complex, or high-risk products and policy- and precedent-setting decisions. When emerging policy or precedent-setting issues are identified, the division director notifies relevant personnel (e.g., Immediate Office, the Office of Generic Drug Policy, the Office of Policy for Pharmaceutical Quality), as appropriate, and works collaboratively to resolve the issues.

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 (except to the extent issues within an amendment are correlated to, and could impact, resolved issues). 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 reassigned the amendment for workload management reasons and 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, FDA will act on the unsolicited amendment by the later of the goal date for the original submission/solicited amendment or the goal date assigned for the unsolicited amendment.

REFERENCES

- CDER MAPP 4151.8 Rev.1 *Equal Voice: Collaboration and Regulatory and Policy Decision-Making in CDER* (Effective Date: 04/12/22)

- FDA Guidance for Industry *Good Abbreviated New Drug Application Submission Practices* (January 2022)

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 identified by a discipline assessor and/or assessment team for its portion of the pending application at the conclusion of the discipline assessment.

- **Complete response letter:** A written communication to an applicant from FDA usually describing all the specific deficiencies that the Agency has identified in an ANDA (including pending amendments) that must be satisfactorily addressed before the ANDA can be approved.

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
1/3/18	Initial	N/A
10/6/2023	1	Updates to account for changes made by GDUFA III