

POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

ANDA Amendments and Supplements Reviewed by the Division of Filing Review

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PURPOSE

This MAPP outlines policies and procedures for the Office of Generic Drugs (OGD), the Center for Drug Evaluation and Research Central Document Room (Document Room), and the Office of Pharmaceutical Quality (OPQ) to determine whether an amendment or supplement should be reviewed by OGD’s Division of Filing Review (DFR).

POLICY

OGD’s DFR reviews each original abbreviated new drug application (ANDA) submitted to OGD to evaluate whether an ANDA may be received or refused for receipt pursuant to FDA’s regulations at 21 CFR 314.101, which provide the regulatory authority by which FDA may in certain cases, and will in others, refuse to receive (RTR) an ANDA.

Receipt of an ANDA means that FDA has made a threshold determination that the ANDA is substantially complete (21 CFR 314.101(b)(1) and 314.3(b)).

In addition to reviewing each original ANDA submitted to OGD to determine if an ANDA may be received, DFR evaluates certain amendments to a pending ANDA and prior approval supplements (PASs) to an approved ANDA to identify deficiencies that, if addressed before assessment by the review disciplines, will streamline the assessment

process. Specifically, DFR evaluates an amendment to a pending ANDA or a PAS, if the submission contains the following changes:

- Additional strength (i.e., a strength other than the one(s) already proposed or approved in the ANDA), including but not limited to an:
 - Additional strength of a solid oral dosage form drug product
 - Additional concentration for a parenterally administered drug product
 - Additional fill volume for a parenterally administered drug product (i.e., total drug content)
 - Additional concentration or strength of an oral liquid, ophthalmic, otic, transdermal, or topical drug product
- Changes to the formulation of any drug product in any dosage form
- Switch of a drug product from prescription to over-the-counter status (Rx-to-OTC switch)
- Change in container closure system for a parenterally administered drug product
- Reintroduction of a strength that has been discontinued or has not been marketed for several years

RESPONSIBILITIES AND PROCEDURES

Document Room Staff will:

- Review the cover letter and Form FDA 356h—in accordance with the attachments to this MAPP—to determine the submission type and applicable coding
 - *For new strength amendments and supplements*
 - Review the cover letter in accordance with the attachments to this MAPP, as needed, for the following key phrase: *new strength added*
 - Review the following fields on Form FDA 356h:
 - Strength
 - Reason for Submission

- Determine the application status
 - If the application is not approved (e.g., if it is pending or in complete response or tentative approval status) and the submission is seeking to add a new strength, perform data entry in the Document Archiving, Reporting, and Regulatory Tracking System (DARRTS) and the CDER Informatics Platform (the Platform) and code the submission as a *Quality/New Strength* amendment
 - If the application is approved and the submission is seeking to add a new strength, perform data entry in DARRTS and code the submission as a *CMC/New Strength* supplement
- *For formulation amendments and supplements*
 - Review the cover letter in accordance with the attachments to this MAPP, as needed, for the following key phrases:¹
 - *Change in formulation*
 - *Updated formulation*
 - *New formulation*
 - Review the following field on Form FDA 356h: Reason for Submission
 - Determine the application status
 - If the application is not approved (e.g., if it is pending or in complete response or tentative approval status) and the submission is seeking to change the formulation, perform data entry in DARRTS and the Platform and code the submission as a *Quality/Formulation Information* amendment
 - If the application is approved and the submission is seeking to change the formulation, perform data entry in DARRTS and the Platform and code the submission as a *CMC/Formulation* supplement
- If the submission does not result in review by DFR based on this MAPP and its attachments, route the submission directly to the OGD regulatory project manager (OGD RPM) or the OPQ regulatory business process manager (OPQ RBPM), as appropriate

¹ See Attachment 1, question 1 for additional phrases.

- Contact the DFR project manager (PM) if additional assistance is needed in identifying whether the submission needs a filing review

OGD RPM and/or OPQ RBPM will:

- For every amendment and supplement the Document Room routes directly to the OGD RPM or OPQ RBPM, review the cover letter during the triage stage in accordance with the checklist (Attachment 1) to confirm that the amendment or supplement was appropriately routed to the OGD RPM or OPQ RBPM
- If the submission does require review by DFR based on this MAPP and its attachments, confirm in the Platform whether a filing review was performed by DFR for the submission
- Contact the DFR PM if a filing review is needed but has not been performed
- Contact the DFR PM if additional assistance is needed in identifying whether the submission needs a filing review

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
11/12/15	Initial	N/A
4/17/2020	1	Revised for minor clarifications and formatting. Added Attachment 2 - Work Guide for Prior Approval Supplements: Requirements for a Filing Review

ATTACHMENT 1: Checklist: Should This Submission be Sent to the Division of Filing Review?

Question	Yes	No
<p>1 Does the cover letter* or Form FDA 356h include any of the following phrases?</p> <ul style="list-style-type: none"> • <i>Addition of</i> • <i>New strength added</i> • <i>Change in formulation</i> • <i>Updated formulation</i> • <i>New formulation</i> • <i>Rx-to-OTC Switch</i> • <i>Container-closure system</i> • <i>Reintroduction</i> • <i>Reactivation</i> 		
<p>2 If the submission is for a solid oral dosage form, are additional strengths of the drug product being proposed?</p>		
<p>3 If the submission is for a parenterally administered drug product, are there any changes in concentration (e.g., milligram/milliliter or percent) and/or fill volume?</p>		
<p>4 If the submission is for an oral liquid, ophthalmic, otic, topical, or transdermal drug product, are there any changes in concentration of the drug product?</p>		
<p>5 For all dosage forms, are there any changes in the formulation?</p>		

*Read the cover letter in its entirety.

If the answer to any of the following questions is “Yes,” route the submission to the Division of Filing Review.

For additional assistance in identifying whether the submission needs a filing review contact the Division of Filing Review Project Manager.

ATTACHMENT 2: Work Guide for Prior Approval Supplements: Requirements for a Filing Review

Requested Change	Route to the Division of Filing Review	Notes
Adding an additional strength	All additional strengths	Additional fill volume is considered an additional strength for parenterally administered drug products.
Changing the formulation	<p>All formulation (quantitative and qualitative) changes that require a prior approval supplement (PAS), such as:</p> <ul style="list-style-type: none"> • Reformulation or new formulation • Increase or decrease in excipient amount • Removal or addition of pH adjuster • Increasing, replacing, or adding a color additive or flavor 	<ul style="list-style-type: none"> • A filing review is not required for changes being effected (CBE) supplements. • A reduction/removal of existing flavor or color additive can be submitted in an annual report; a filing review is not required.
Adding a new formulation	All new formulations (e.g., preservative vs. non-preservative)	Additional formulations may be included in the same application as the original approved formulation, if the reference listed drug provides for multiple formulations under a single new drug application.
Rx to OTC switch	All Rx to OTC switches	
Changing the container closure system for parenterally administered drug products	<ul style="list-style-type: none"> • If a change is for an injectable. • If the container closure system change is accompanied by a new strength or a proposed formulation change. 	If multiple container closure systems for a parenterally administered drug product are covered under a single new drug application, then an abbreviated new drug application may submit a PAS

	<ul style="list-style-type: none"> If a new container closure system is <i>added</i> to an ANDA for a parenterally administered drug product. 	<p>for the addition of a container closure system.</p>
<p>Reintroducing a strength that has been discontinued/has not been marketed in several years</p>	<ul style="list-style-type: none"> If commercial production has been restarted by adding a new manufacturing site. 	<ul style="list-style-type: none"> A restart at a new manufacturing site of a type of operation that has been discontinued for more than two years will require a PAS. If the criterion above is not met, the assessment team should conduct a case-by-case evaluation to see if the change may be appropriately submitted as a CBE supplement rather than a PAS. If a CBE supplement is appropriate, a filing review is not needed.