
POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

**Generic Drug Labeling Revisions Under
Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act**

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PURPOSE

This Manual of Policies and Procedures (MAPP) describes how the Office of Generic Drugs (OGD) will implement section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).¹

BACKGROUND

On March 23, 2010, the President signed into law H.R. 3590, the Patient Protection and Affordable Care Act. Section 10609 of that Act added section 505(j)(10) to the FD&C

¹ See 21 U.S.C. 355(j)(10).

Act. Section 505(j)(10) permits the Food and Drug Administration (FDA) to approve an abbreviated new drug application (ANDA) with labeling that temporarily differs from that of the reference listed drug (RLD) when certain changes to the labeling for the RLD have recently been approved.

On December 29, 2022, the President signed into law H.R. 2617, the Consolidated Appropriations Act, 2023. Section 3224 of that Act amended section 505(j)(10) of the FD&C Act² to expand the RLD labeling revisions to which the provisions of this section apply from certain changes made within 60 days of an ANDA being otherwise eligible for approval but for expiration of a patent, exclusivity period, or a delay of approval described in section 505(j)(5)(B)(iii) of the FD&C Act,³ to certain changes approved within 90 days of when an ANDA is otherwise eligible for approval. The law was also amended to require that the ANDA sponsor agree to submit revised labeling within 60 days of the date of ANDA approval, rather than within 60 days after the notification of any changes to such labeling from FDA.

If, prior to approval, the ANDA labeling does not reflect labeling changes recently approved for the RLD and after receiving a request by an ANDA applicant to determine whether the ANDA meets the criteria to be eligible for approval subject to this section, FDA will send the applicant a General Advice Notification letter notifying the applicant of the RLD labeling changes and asking the applicant to commit, in a Letter of Commitment submitted to FDA, to submit the revised labeling within 60 calendar days of the date of ANDA approval. By submitting a Letter of Commitment, the applicant agrees to the requirement in section 505(j)(10) of the FD&C Act to update its labeling no later than 60 calendar days after the date of ANDA approval.

POLICY

- Under section 505(j)(10) of the FD&C Act, FDA may approve an ANDA, even though certain changes have been made to the labeling for the RLD and such changes are not included in the proposed labeling of the ANDA, if all the following criteria are met:
 - The ANDA is otherwise eligible for approval and FDA has approved the RLD’s labeling revision within 90 calendar days of such eligibility for approval.

² See Division FF, Title III, Subtitle B, Chapter 2, Section 3224 of the Consolidated Appropriations Act, 2023 (P.L. 117-328).

³ This clause in the FD&C Act describes a statutory stay of approval that generally extends for 30 months but can be terminated early by a court entry of judgment of non-infringement or invalidity of the relevant patent(s).

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- The approved revisions to the labeling of the RLD did not include a change to the “Warnings” section of the labeling.⁴
 - The ANDA applicant has agreed, in a Letter of Commitment, to submit a “Supplement – Changes Being Effected” containing the revised labeling consistent with the changes made to the labeling for the RLD no later than 60 calendar days after the date of ANDA approval.
 - FDA has determined that the applicant’s continued use of the RLD labeling that was in effect before the RLD revision will not adversely impact the safe use of the proposed generic drug product.⁵
 - FDA will not grant final approval of an ANDA until the applicant’s Letter of Commitment is received.
 - If at any point the ANDA under consideration is determined to no longer be “otherwise eligible for approval” (e.g., due to a deficiency identified in the application), FDA will cease the procedures noted below and provide notice that the ANDA is not eligible for approval through the appropriate standard form of communication.

RESPONSIBILITIES

- Any OGD staff member receiving a request by an ANDA applicant to determine whether the ANDA is eligible for approval, despite labeling changes approved for the RLD and the proposed ANDA labeling does not yet include those labeling changes, will send that request to the appropriate Labeling Project Manager (LPM) in the Division of Labeling Review (DLR).
- DLR Labeling Assessor (LA):
 - Recommends whether the labeling changes approved for the RLD meet the criteria under section 505(j)(10) and requests approval of that recommendation from the DLR Team Leader (TL). This includes confirming with the Division of Project Management (DPM) RPM that all discipline reviews are adequate.

⁴ Please note that the physician labeling rule (PLR) consolidates the “Warnings and Precautions” sections. For more information on PLR, please visit FDA’s website on Prescription Drug Labeling Resources at: <https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources>.

⁵ OGD may contact the Office of New Drugs (OND) to determine if the labeling revision impacts the safe use of the drug.

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- Consults with the Patent and Exclusivity Team (PET) within OGD Policy for assistance in determining if the ANDA is eligible for final or tentative approval when there are patent(s) and/or exclusivity issues.
 - With the assistance of the DLR LPM, DLR LA completes a memorandum in the electronic archiving system used in the Center for Drug Evaluation and Research (CDER) documenting the section 505(j)(10) determination under the Labeling Review Task.

 - Consults the appropriate OND review division, as necessary, to determine if the applicant's continued use of the RLD labeling that was in effect before the RLD revision will not adversely impact the safe use of the proposed generic drug product.

 - DLR LPM:
 - Ensures appropriate DLR staff are aware that a request under section 505(j)(10) has been received.
 - Requests the DLR LA determine whether the labeling changes approved for the RLD meet the criteria under section 505(j)(10).
 - If the DLR staff determine that all criteria under section 505(j)(10) are met and the request is to be granted, prepares a General Advice Notification letter via the electronic archiving system used in CDER and issues that letter to the applicant after it is signed by the DLR TL.
 - If the DLR staff determine that the criteria have not been met and the request is to be denied, prepares and issues a communication to ANDA applicants that have requested a 505(j)(10) determination from FDA indicating that the criteria under section 505(j)(10) are not met.
 - Communicates the section 505(j)(10) determination to the DPM RPM via CDER's electronic archiving system through an update under the Labeling Review Recommendation.
 - Verifies the Letter of Commitment has been received from the applicant and the memorandum to file (e.g., example template available in Attachment 4) has been completed in the electronic archiving system used in CDER.
 - Tracks status of post-approval labeling requirements (PALRs) monthly.
 - Ensures the required "Supplement – Changes Being Effected" is submitted within 60 calendar days of the date of ANDA approval.
 - For supplements received within 60 calendar days:

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- Within 5 calendar days, issues a Post-Approval Labeling Requirement Released Letter at the program level.
 - When a supplement is not received within 60 calendar days:
 - Within 5 calendar days, issues a Post-Approval Labeling Requirement Failure to Respond Letter to any ANDA applicant that fails to submit the labeling supplement within 60 calendar days from the date of ANDA approval.
 - Notifies DPM RPM of the failure to submit the labeling supplement.
 - Notifies PET and the ORO IO if FDA issues a Post-Approval Labeling Requirement Failure to Respond Letter to any ANDA applicant that fails to submit the labeling supplement within 60 calendar days from the date of ANDA approval.
 - DLR TL:
 - Verifies the recommendation of the DLR LA that the labeling changes approved for the RLD meet the criteria under section 505(j)(10) and the ANDA applicant is eligible for approval, notwithstanding the labeling considerations described under section 505(j)(10).
 - Signs a General Advice Notification letter to the ANDA applicant on behalf of the DLR Division Director, which is drafted by the DLR LPM.
 - Prior to final approval of the ANDA, verifies the Letter of Commitment has been received and the memorandum under the Labeling Review Task has been completed.
 - Asks the DPM RPM or the Office of Regulatory Operations (ORO) Immediate Office (IO) to include language memorializing the PALR to submit revised labeling in the approval letter if it was not already added. This will be completed during the labeling endorsement stage when the ANDA is being routed for final approval.
 - DPM RPM:
 - Triages section 505(j)(10) requests received via the electronic gateway as Administrative Amendments and verifies that all relevant discipline reviews are final and adequate to determine whether the ANDA is otherwise eligible for approval despite labeling changes approved for the RLD and forwards requests to the appropriate DLR LPM.

- Ensures the language memorializing the PALR to submit revised labeling is included in the approval letter if it was not already added.
 - Triage and forwards incoming Letters of Commitment to the DLR LPM as an Administrative Amendment.

 - Adds comments regarding receipt of the Letter of Commitment to the approval routing summary (ARS) during the routing of the ANDA for final approval, thereby alerting the ORO IO of the applicant's commitment to submit revised labeling for its proposed generic drug product corresponding to the RLD labeling changes within the specified timeframe.

 - Informs the DLR LPM via email when the ANDA is approved.

 - If necessary, initiates withdrawal of approval of the application after receiving notification from the DLR LPM that more than 60 calendar days had lapsed from the date of ANDA approval, and the applicant was sent the Post-Approval Labeling Requirement Failure to Respond Letter and continued to fail to submit the labeling supplement. Notifies PET when such an action is initiated.
- ORO IO:
 - Confirms receipt of the Letter of Commitment from the applicant and documentation on the ARS of the applicant's commitment to submit revised labeling through a "Supplement – Changes Being Effected" within 60 calendar days of the date of ANDA approval.

 - Ensures the final approval letter for the ANDA includes language requiring the applicant to revise, within 60 calendar days of the date of ANDA approval, the labeling of its product to conform to the revisions approved for the RLD.
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PROCEDURES

- **Determination**
 - Once the ANDA applicant becomes aware that a revision to the RLD labeling has been approved that meets the statutory criteria under section 505(j)(10), as described in the Policy section, the applicant may request a determination whether to invoke section 505(j)(10).
 - Upon receipt of a request from an ANDA applicant via the electronic gateway for a determination of eligibility for approval subject to section 505(j)(10), DPM RPM triages the request to the DLR LPM as an

Administrative Amendment. The DLR LPM will ensure all relevant parties are aware of the submission and request a determination of eligibility from the DLR LA.

- The DLR LA determines whether the criteria under section 505(j)(10) are met, and with the assistance of the DLR LPM, both (1) completes a memorandum in CDER's electronic archiving system documenting that recommendation under the Labeling Review Task (see Attachment 4) and (2) requests concurrence from the DLR TL with that determination.
 - The DLR TL verifies whether the DLR LA's recommendation regarding the determination that the criteria under section 505(j)(10) are met. If the DLR TL agrees with the DLR LA's recommendation, then the DLR TL signs the memorandum documenting concurrence (see Attachment 4). If the DLR LA and DLR TL are not in agreement about that determination, they will consult the DLR Supervisor for resolution. Documentation of the final determination is archived in CDER's electronic archiving system.
 - The DLR LPM notifies the DPM RPM of the determination.
- **Processing**
 - If the DLR staff determine that all criteria under section 505(j)(10) are met, the DLR LPM will prepare and issue a General Advice Notification letter signed by the DLR TL to the applicant or its authorized agent(s) via email through the electronic archiving system used in CDER (see Attachment 1). The General Advice Notification letter will request that the applicant submit a Letter of Commitment to FDA, in which the applicant agrees to submit a "Supplement – Changes Being Effected" within 60 calendar days of the date of ANDA approval.
 - If the DLR staff determine the criteria under section 505(j)(10) are not met and the request should therefore be denied, the DLR LPM will create and issue a communication to ANDA applicants that have requested a section 505(j)(10) determination from FDA indicating that the criteria under section 505(j)(10) are not met (see Attachment 1).
 - After the Letter of Commitment is received from the applicant, the DLR LPM will update the memorandum under the Labeling Review Task with the PALR information.
 - At the time of labeling endorsement for final approval of the ANDA, the DLR TL:
 - Verifies the Letter of Commitment has been received and the memorandum under the Labeling Review Task has been completed.

- Asks the DPM RPM or the ORO IO to include language memorializing the PALR to submit revised labeling in the approval letter if it was not already added (see Attachment 2).
 - Once FDA receives the applicant’s Letter of Commitment, the DPM RPM and/or the ORO IO staff includes language memorializing the PALR to submit revised labeling in the approval letter (see Attachment 2) and document the PALR on the OGD Approval Routing Summary form.
 - **Tracking Commitment**
 - The DLR LPM uses CDER’s electronic archiving system to track the applicant’s fulfillment of the PALR to submit revised labeling as a “Supplement – Changes Being Effected” within 60 calendar days of the date of ANDA approval.
 - The DPM RPM informs the DLR LPM via email when the ANDA is approved.
 - The DLR LPM tracks status of PALRs monthly.
 - Based on the date of ANDA approval, the DLR LPM tracks the required submission date for revised labeling (which is due within 60 calendar days of the date of ANDA approval).
 - Once the applicant submits a timely “Supplement – Changes Being Effected” with the revised labeling, the DLR LPM issues a Post-Approval Labeling Requirement Released Letter and document it in CDER’s electronic archiving system (see Attachment 3).
 - **Failure to Respond**
 - The DLR LPM issues a Post-Approval Labeling Requirement Failure to Respond Letter to any ANDA applicant that fails to submit the labeling supplement within 60 calendar days from the date of ANDA approval (see Attachment 5). The Post-Approval Labeling Requirement Failure to Respond Letter will state that timely changes to the labeling were required as a condition of approval and, if necessary, FDA will begin withdrawal of approval of the application.
 - The DLR LPM notifies PET and the ORO IO.
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REFERENCE

- Patient Protection and Affordable Care Act (Public Law 111-148) (<http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf>)
- Consolidated Appropriations Act, 2023 (P.L. 117-328): (<https://www.congress.gov/bill/117th-congress/house-bill/2617>)

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
02/12/2013	N/A	Initial
07/27/2021	1	Procedures updated
12/13/2023	2	Updates to account for changes made by P.L. 117-328 (2022)

**ATTACHMENT 1 – Sample Letter - General Notification Template
(Denied/Granted)**

ANDA #####

GENERAL ADVICE NOTIFICATION

Applicant or US Agent Name
U.S. Agent for: Applicant Name
Applicant or US Agent Address 1
Applicant or US Agent Address 2
Applicant or US Agent Address 3

Attention: CONTACT NAME
TITLE

Dear CONTACT:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on DATE, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for TRADE NAME, IF GIVEN, (ESTABLISHED NAME) DOSAGE FORM AND STRENGTH(S).

Reference is also made to your request to invoke section 505(j)(10) of the FD&C Act.

The Food and Drug Administration (FDA) approved new labeling for the reference listed drug (RLD), insert [NDA XXXXXX, RLD TRADE NAME, DOSAGE FORM, AND STRENGTH(S)], on insert date. Section 505(j)(10) of the FD&C Act permits FDA to approve an ANDA with labeling that differs from that of the RLD provided: (1) the application is otherwise eligible for approval and FDA has approved a revision to the labeling of the RLD within 90 days of when your ANDA is otherwise eligible for approval, (2) the labeling changes do not include a change to the “Warnings” section, (3) FDA has determined that the continued presence of the labeling in effect before the revision will not adversely impact the safe use of the drug, and (4) the applicant agrees to submit revised drug labeling no later than 60 days after ANDA approval.

OPTION A:

We have determined that the drug under your ANDA meets the criteria under section 505(j)(10), provided that you agree to supplement your application with updated labeling reflecting the change to the insert name of RLD labeling within 60 days of the date of ANDA approval. Your commitment in writing should be identified as a “Letter of

Commitment to Submit Revised Labeling Pursuant to 505(j)(10)” and submitted via the Electronic Submissions Gateway (ESG).⁶

Please note that this commitment letter must be received before approval of your application can be granted.

When submitting your supplement with updated labeling to reflect the change to the *insert name of RLD* labeling, identify your supplement as:

**CBE SUPPLEMENT
LABELING
POST-APPROVAL COMMITMENT – MET**

Your supplement must be submitted in Electronic Common Technical Document (eCTD) format. The eCTD is CDER’s standard format for electronic regulatory submissions. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd.

OPTION B:

We have determined that the drug under your ANDA does not meet the criteria under section 505(j)(10), due to (list reason).

You are required to amend your pending application to align your labeling with the recent NDA supplement approval prior to approval of your application. This submission will receive a minor amendment GDUFA date of three months from date of receipt.

Your amendment must be submitted in Electronic Common Technical Document (eCTD) format. The eCTD is CDER’s standard format for electronic regulatory submissions. Submissions that do not adhere to the requirements stated in the eCTD Guidance will be subject to rejection. For more information please visit: www.fda.gov/ectd. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission.

**MINOR AMENDMENT
LABELING**

If you have questions, please contact (LPM) via email at (email address).

Sincerely Yours,

{See appended electronic signature page}

⁶ See FDA’s guidance for industry “*ANDA Submissions —Content and Format*” (Rev. 1) (September 2018), available at: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

For xx
Director
Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

ATTACHMENT 2 - Standard Language for Approval Letter**POST-APPROVAL LABELING REQUIREMENT UNDER SECTION 505(j)(10)**

We remind you of your post-approval labeling requirement (PALR).

FDA approved a revision to the labeling of the RLD within 90 days of when your ANDA was otherwise eligible for approval. This revision to the labeling of the RLD does not include a change to the “Warnings” section, and the agency has determined that the continued presence of the labeling in effect before the revision will not adversely impact the safe use of the drug.

The agency has also determined that your ANDA meets the applicable standards for approval, subject to section 505(j)(10) of the FD&C Act and is otherwise eligible for approval. Therefore, subject to section 505(j)(10) of the FD&C Act, your ANDA is eligible for approval with labeling that differs from that of the RLD. As indicated in the General Advice Notification letter dated xx/xx/xxxx, you are required to submit revised labeling for your product to conform to the revision that was approved on _____ *insert date for the RLD* _____ for _____ *insert RLD's name* _____. As agreed to in the Letter of Commitment, you are required to submit a “Supplement – Changes Being Effected” containing such revised labeling no later than 60 days after the date of ANDA approval.

ATTACHMENT 3 - Standard Language for Release from Post-Approval Labeling Requirement

POST-APPROVAL LABELING REQUIREMENT UNDER SECTION 505(j)(10)

We acknowledge receipt of your “Supplement – Changes Being Effected” on insert date. As indicated in the General Advice Notification letter dated xx/xx/xxxx and the ANDA approval letter dated xx/xx/xxxx, you were required to change the labeling of your product to conform to the revisions that were approved on _____ insert date for the RLD _____ for _____ insert RLD’s name _____. You agreed to submit a “Supplement – Changes Being Effected” containing revised labeling no later than 60 days after the date of ANDA approval, which constituted a Post-Approval Labeling Requirement (PALR).

As you have now submitted a “Supplement – Changes Being Effected” containing revised labeling, you are hereby released from your PALR as of the date of this letter.

ATTACHMENT 4 – Memorandum to File – Documenting Decision

Determination whether an ANDA meets the criteria described in section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Background information

Section 505(j)(10) of the FD&C Act permits FDA to approve an ANDA with labeling that differs from that of the RLD provided: (1) the application is otherwise eligible for approval and FDA has approved a revision to the labeling of the RLD within 90 days of such eligibility for approval, (2) the labeling changes do not include a change to the “Warnings” section, (3) the ANDA applicant(s) agrees to submit revised labeling no later than 60 days after ANDA approval, and (4) FDA has determined that the continued presence of the labeling in effect before the revision will not adversely impact the safe use of the drug.

NDA Number	
Product Name	
ANDA Applicant Name	
ANDA #	
Approval of the revision of the labeling for the RLD has been made within 90 days of when the ANDA was otherwise eligible for approval: 1. Date RLD labeling was approved: 2. Date ANDA was otherwise eligible for approval:	<input type="checkbox"/> Yes <input type="checkbox"/> No
Has DLR verified the approved revisions to the RLD labeling do not include a change to the “Warnings” section?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Has the applicant committed to submit revised labeling to reflect the change in the labeling of the RLD no later than 60 days after ANDA approval?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Has FDA determined that the continued presence of the labeling in effect before the revision will not adversely impact the safe use of the drug?	<input type="checkbox"/> Yes <input type="checkbox"/> No
FINAL DECISION: Can this ANDA be approved with certain labeling differences from that of the RLD as described in section 505(j)(10) of the FD&C Act?	<input type="checkbox"/> Yes <input type="checkbox"/> No

{See appended electronic signature}
 Labeling Reviewer

Supervisory Comment/Concurrence:

{See appended electronic signature}
Team Leader

ATTACHMENT 5 – Sample Letter Template – Failure to Respond to Supplement Request

ANDA #####

**REQUEST RESPONSE TO
SUPPLEMENT REQUEST**

APPLICANT NAME
APPLICANT ADDRESS
Attention: NAME OF CONTACT PERSON
TITLE

Dear CONTACT:

Please refer to your abbreviated new drug application (ANDA) approved under section 505(j) of the Federal Food, Drug, and Cosmetic Act for TRADE NAME IF GIVEN, (ESTABLISHED NAME) DOSAGE FORM AND STRENGTH(S).

A CHANGES BEING EFFECTED LABELING SUPPLEMENT IS REQUIRED

As indicated in the General Advice Notification letter dated xx/xx/xxxx and the ANDA approval letter dated xx/xx/xxxx, you were required to change the labeling of your product to conform to the revisions that were approved on _____ *insert date for the RLD* _____ for _____ *insert RLD's name* _____. You agreed to submit a “Supplement – Changes Being Effected” containing revised labeling no later than 60 days after ANDA approval, which constituted a Post-Approval Labeling Requirement (PALR).

To date we have not received a “Supplement – Changes Being Effected” containing revised labeling. If you do not submit the required supplement, this drug product may be considered misbranded, and, if necessary, FDA will begin withdrawal of approval of the application.

If you have questions, please contact (LPM) via email at (email address).

Sincerely,

{See appended electronic signature page}

For xx
Director
Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research