POLICY AND PROCEDURES

OFFICE OF GENERIC DRUGS

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

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PURPOSE

- This MAPP describes how the staff in the Office of Generic Drugs (OGD) should implement section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

BACKGROUND

- On March 23, 2010, the President signed into law H.R. 3590, the Patient Protection and Affordable Care Act (the PPACA). Section 10609 of the PPACA added section 505(j)(10) to the FD&C Act. This section permits the Food and Drug Administration (FDA) to approve an abbreviated new drug application (ANDA) even if the approval coincides with certain changes to the labeling for the reference listed drug (RLD), as long as the ANDA applicant agrees to submit revised labeling corresponding to the RLD labeling changes within 60 days of notification of the change.

POLICY

- FDA may approve an ANDA, even though certain changes have been made to the labeling for the RLD, if all of the following criteria are met:
    - The approval of the RLD's labeling revision is made within 60 days before the expiration of a listed patent, an exclusivity period, or a 30-month stay delaying ANDA approval.
    - The approved revision to the labeling of the RLD does not include a change to the "Warnings" section (the physician labeling rule format consolidates the "Warnings and Precautions" sections).
    - 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 product.
- The ANDA sponsor(s) must provide a letter of commitment to submit a "Supplement – Changes Being Effected" containing the revised labeling no later than 60 days after the date of notification by FDA.
- The labeling project manager (PM) will use the FDA Document Archiving Reporting and Regulatory Tracking System (DARRTS) to track the fulfillment of agreements to submit revised labeling as a supplement within the specified time frame.

RESPONSIBILITIES

- Labeling Review Branch (LRB) Reviewer:
    - Evaluates whether the labeling change(s) approved for the RLD meet the criteria under section 505(j)(10) of the FD&C Act.
    - Communicates the decision to the ANDA applicant that specifies all required follow-up actions.
- Team Leader:

  Verifies whether the reviewer's recommendation that the sponsor(s) should be granted a 60-day grace period to submit the generic drug labeling revisions meets the criteria described in section 505(j)(10). Ensures the provision is consistently applied.
- Product Quality Review Project Manager (PQRPM):

Ensures the standard language for generic drug labeling revisions described under section 505(j)(10) has been included in the letter.

- Labeling Project Manager (LPM):

  Enters the ANDA sponsor's agreement in the DARRTS tracking system. Ensures the agreements are addressed in the appropriate time frame.

PROCEDURES

Determination

- Unless the ANDA applicant submits revised labeling prior to approval, the ANDA sponsor(s) or an OGD staff member may request a 60-day grace period to submit generic drug labeling revisions described by section 505(j)(10) of the FD&C Act.

- The LRB reviewer evaluates whether the criteria under section 505(j)(10) are met.

- The team leader ascertains whether the reviewer's recommendations are appropriate. If the reviewer and team leader are not able to agree, they will bring their concerns to the director of the Division of Labeling and Program Support for resolution.

Processing

- If the labeling reviewer and team leader determine that the criteria under section 505(j)(10) are met, the labeling reviewer will issue a letter to the ANDA sponsor(s) requesting a commitment to update the labeling within 60 days of notification (Attachment A). In cases where the letter to the ANDA sponsor(s) requesting a commitment would not reach the sponsor(s) before the date the drug product is eligible for approval, the labeling reviewer will contact the ANDA sponsor(s) by email or phone and follow up by sending a letter requesting the commitment.

- At the time of labeling endorsement for final approval of the ANDA, the labeling reviewer will:

    - Ask the PQRPM to include postmarket labeling agreement language in the approval letter if it had not been added (Attachment B).

    - Include a memorandum in DARRTS documenting the decision (Attachment C).

- The PQRPM includes postmarket labeling agreement language in the approval letter and checks the box for "Labeling Agreement" on the OGD Approval Routing Summary form.

Tracking Commitment

- The PQRPM informs the Labeling Reviewer via email when the ANDA is approved. The Labeling Reviewer completes the postmarket commitment form (Attachment D) and emails the form to the LPM.

- The LPM enters the agreement into DARRTS.

- The LPM tracks labeling postmarket agreements on a monthly basis.

- The LPM contacts ANDA sponsor(s) who fail to submit the labeling supplement within 60 calendar days from the date of notification and informs them that such changes to the labeling are required as a condition of approval.

REFERENCE

- Patient Protection and Affordable Care Act (Public Law 111-148). (http://www.gpo.gov/fdsys/pkg/PLAW-111publ148/pdf/PLAW-111publ148.pdf)

EFFECTIVE DATE

This MAPP is effective upon date of publication.

ATTACHMENT A - Sample Letter - Request Letter of Commitment

Application Number

Address

Dear :

This is in reference to your abbreviated new drug application (ANDA) dated _*insert date*_____, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for __*insert name of drug product*_____.

Reference is also made to your amendments dated __*insert date*____.

FDA approved new labeling for the reference listed drug (RLD),_*insert name of RLD* , on_*insert date*. The (specify *'### patent, pediatric exclusivity period attached to the '### patent, 3-year exclusivity period under section 505(j)(5)(F)(iii)-(iv) of the FD&C Act, 180-day exclusivity period under section 505(j)(5)(B)(iv) of the FD&C Act, orphan exclusivity period under section 527 of the FD&C Act, or 30-month stay of approval*) is scheduled to expire on ___*add expiration date*. The FD&C Act, section 505(j)(10) (added by section 10609 of the Patient Protection and Affordable Care Act) permits FDA to approve an ANDA with labeling that differs from that of the RLD provided: (1) the change to the RLD labeling is approved within 60 days of the expiration of a listed patent, an exclusivity period, or 30-month stay, and the labeling changes do not include a change to the "Warnings" section, (2) 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 (3) the applicant agrees to submit revised drug labeling no later than 60 days after being notified of the required changes.

Under section 505(j)(10), we can approve your ___*insert name of drug product* ANDA provided you commit to supplementing your application with updated labeling reflecting the change to the ___*insert name of RLD* labeling within 60 days of your receipt of notification (i.e., today's date). Your commitment in writing may be submitted electronically via the Electronic Submissions Gateway (ESG), faxed followed by a hard-copy, or mailed to:

Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North VII
7620 Standish Place
Rockville, MD 20855

Please note that this commitment letter must be received before full approval of your drug product can be granted. Thank you in advance for your prompt attention regarding this matter.

Sincerely Yours,

{See appended electronic signature page}

Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ATTACHMENT B - Standard Language for Approval Letter

FDA approved a revision to the labeling of the RLD within 60 days of the expiration of the ____*insert '### patent, pediatric exclusivity period attached to the '### patent, 3-year exclusivity period under section 505(j)(5)(F)(iii)-(iv) of the FD&C Act, 180-day exclusivity period under section 505(j)(5)(B)(iv) of the FD&C Act, orphan exclusivity period under section 527 of the FD&C Act, or 30-month stay of 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 under section 505(j), and was otherwise eligible for approval but for expiration of the _____*insert '### patent, pediatric exclusivity period attached to the '### patent, 3-year exclusivity period under section 505(j)(5)(F)(iii)-(iv) of the FD&C Act, 180-day exclusivity period under section 505(j)(5)(B)(iv) of the FD&C Act, orphan exclusivity period under section 527 of the FD&C Act, or 30-month stay of approval*_____. Therefore, under section 505(j)(10) of the FD&C Act, your ANDA is eligible for approval with labeling that differs from that of the RLD. You are hereby notified that you are required to change the labeling of your product to contain the revision that was approved on _____*insert date for the RLD*_____ for _____*insert RLD's name*___. Acceptance of this letter constitutes your agreement to submit a "Supplement – Changes Being Effected" containing such revised labeling no later than 60 days after the date of the notification.

ATTACHMENT C - Memorandum to File - Documenting Decision

Determination if generic drug labeling meets the criteria described in section 505(j)(10) of the Food, Drug, and Cosmetic Act (FD&C Act)

Approval of the revision of the labeling for the RLD has been made within 60 days before the expiration of a listed patent, an exclusivity period, or a 30-month stay delaying ANDA approval: 1. NDA #: 2. NDA product name (trade and established): 3. Date RLD labeling was approved: 4. Expiration date of listed patent, exclusivity period, or a 30-month stay delaying ANDA approval.	☐ Yes ☐ No
Does the approved revision to the RLD labeling include a change to the "Warnings" section?	☐ Yes ☐ No
Has the sponsor(s) of the application agreed to submit revised labeling of the drug to reflect the change in the labeling of the RLD no later than 60 days after receiving notification that the changes are required?	☐ Yes ☐ No
Has FDA determined that the continued presence of the labeling in effect before the revision will adversely impact the safe use of the drug?	☐ Yes ☐ No **If yes, please explain**:
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?	☐ **Yes** ☐ **No**

Background information

Section 505 (j)(10) of the FD&C Act (added by section 10609 of the Patient Protection and Affordable Care Act) permits FDA to approve an ANDA with labeling that differs from that of the RLD provided: (1) the change to the RLD labeling is approved within 60 days of the expiration of a listed patent, an exclusivity period, or a 30-month stay, and the labeling changes do not include a change to the "Warnings" section, (2) the sponsor(s) of the application agrees to submit revised labeling of the drug no later than 60 days after notification that such changes to labeling are required, and (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.

ATTACHMENT D - Approved ANDA with Required Postmarketing Labeling Commitment

Instructions:

Labeling Reviewer:

Upon approval of the ANDA, fill out this form and send it (via email) to the labeling project manager.

Labeling Project Manager:

Receive the email from the Labeling Reviewer and enter the following agreement information into DARRTS.

Labeling Reviewer:	
Date of Approval:	
ANDA Number:	
Product Name:	
Applicant Name:	
Date of Notification	
Commitment:	ANDA sponsor's commitment to submit a "Supplement – Changes Being Effected" containing revised labeling to be in accord with the labeling approved for the RLD [*insert date of approval*].
Timeframe firm has agreed to submit labeling supplement	60 days from the date of notification

For __*insert name of RLD*___, FDA approved a change to the section__*insert section(s)* of the insert labeling on _____*insert date*_____. The labeling change addresses__ _*describe change*_____. A summary of the changes is provided below.

S-###, Approved__*insert date*
Describe changes

__*Insert the name of the specific ANDA applicant* has committed to supplement its ANDA with revised labeling no later than 60 days after the date it was notified that such a change is required. See letter of commitment dated ___*insert date*.

{See appended electronic signature}

Labeling Reviewer

Supervisory Comment/Concurrence:

{See appended electronic signature}

Team Leader

ATTACHMENT E - Flow Chart

Generic Drug Labeling Revisions Covered Under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

The determination of whether certain generic drug labeling revisions are covered under section 505(j)(10) of the FD&C Act is usually initiated at the request of an abbreviated new drug application (ANDA) sponsor or an Office of Generic Drugs (OGD) staff member.

DETERMINATION

Labeling Review Branch reviewer evaluates if all the following criteria under Section 505(j)(10) are met:

- The approval of the revision to the labeling of the RLD is made within 60 days before the expiration of a listed patent, an exclusivity period, or a 30-month stay delaying ANDA approval.
- The approved revision to the labeling of the RLD does not include a change to the "Warnings" section (Note: in the physician labeling rule format, the "Warnings and Precautions" sections are consolidated).
- 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.

Team leader verifies the reviewer's recommendation is permitted under section 505 (j)(10) and ensures the provision is consistently applied. If the reviewer and team leader are not able to reach agreement, the concerns will be brought to the division director's attention.

RLD labeling changes meet section 505(j)(10) criteria?

No

ANDA sponsor must revise their labeling to be in accord with the RLD labeling prior to approval.

Yes

PROCESSING

Labeling reviewer informs applicants of recent labeling changes to the RLD via letter, email, or by phone and requests a letter of commitment (Attachment A).

At the time of labeling endorsement for final approval of the ANDA:

Labeling Reviewer

- Asks the chemistry project manager to include postmarket labeling agreement language in the approval letter (Attachment B)
- Includes a memorandum in DARRTS documenting the decision (Attachment C)

Product Quality Review Project Manager (PQRPM)

- Includes postmarket labeling agreement language in the approval letter
- Checks the box for "Labeling Agreement" on the OGD Approval Routing Summary form.

ANDA APPROVED AND TRACKING OF COMMITMENT

PQRPM

- Informs the Labeling Reviewer via email when the ANDA is approved.

Labeling Reviewer

- The Labeling Reviewer completes the postmarket commitment form (see Attachment D) and emails the form to the Labeling Project Manager (LPM)

LPM

- Enters the agreement into DARRTS
- Tracks labeling postmarket agreement on a monthly basis