U.S. FOOD & DRUG ADMINISTRATION

Best Practices for Generic Drug Labeling

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Learning Objectives

- Discuss best practices to update abbreviated new drug application (ANDA) labeling following revisions to the approved labeling of a reference listed drug (RLD).
- Review best practices for addressing patents and exclusivities as it relates to generic drug labeling.
- Provide updates on the current best practices on distributing electronic labeling.

Updating ANDA Labeling Following Revision of the RLD Labeling

Background

- Generic drugs are required to have the same labeling as the RLD, except for differences allowed under Section 505(j)(2)(A)(v) of the Act and 21 CFR 314.94(a)(8).
- Applicant expected to update labeling *at the earliest time possible* after FDA has approved labeling for the corresponding RLD.

Labeling Updates for Non-Marketed ANDAs

- Labeling for non-marketed ANDAs that are not withdrawn must also be the same as the most recently approved RLD label.
- If the RLD is withdrawn, refer to the draft guidance titled "Updating ANDA Labeling after the Marketing Application for the Reference Listed Drug has been Withdrawn".

Physician Labeling Rule (PLR)

- Generic drugs must update their labeling to be in PLR format when the RLD labeling is approved with PLR format.
- PLR format labeling:
  - Communicates accurate and up-to-date information on the safe and effective use of drugs,
  - Reduces the number of adverse reactions resulting from medication errors due to misunderstood or incorrectly applied drug information, and
  - Makes the PI more accessible for use with electronic prescribing tools and other electronic information resources.

Where to Find Information on Changes to RLD Labeling

- Drugs@FDA lists recently approved RLD labeling
- Subscribe to *CDER Drug Safety Labeling Changes* and *CDER New* email updates
  - https://www.fda.gov/about-fda/contact-fda/get-email-updates

How to Submit Updated ANDA Labeling

- Unapproved ANDAs: submit an amendment
  - ANDA Submissions – Amendments to Abbreviated New Drug Applications Under GDUFA
- Tentatively approved ANDAs: submit an amendment
  - ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs
- Approved ANDAs: submit a changes being effected (CBE) supplement
  - Changes to an Approved NDA or ANDA

Challenge Question #1

Which resource should be used to find the last approved labeling for the RLD?

A. DailyMed

B. Orange Book

C. Drugs@FDA

D. USP-NF

Addressing Patents & Exclusivities

Disclaimer: the following section reviews best practices for addressing patents and exclusivities as it relates to generic drug labeling.

Patent Certifications

- If there are no patents listed in the Orange Book, or if the patents have expired, the applicant must submit one of the following:
  - Paragraph I certification, paragraph II certification, or a statement that there are no relevant patents
- For each *unexpired* patent listed in the Orange Book, the applicant must provide the patent number and submit one of the following:
  - Paragraph III certification, paragraph IV certification, or a section viii statement

New Patent Use Codes

- Need to address any new, timely filed patent use code(s) when added to an existing patent
  - **New** PIII or PIV certification,
  - or **new** section viii statement
- Reference to a previously submitted certification is **not** sufficient

Exclusivities

For approved ANDAs:

- New labeling carve-outs due to exclusivities should be submitted as a prior approval supplement (PAS).
- Labeling carve-outs to align with an Agency-issued BPCA template should be submitted as a CBE.
- Submission should include a statement addressing the new exclusivity(ies) to clearly state intent.

Patent Certifications and Exclusivities

- Include a screenshot of the Orange Book listing patents and exclusivities for the RLD.
- Submit a patent and exclusivity table under module 1.3.5 listing how each patent and exclusivity is addressed.
- Certifications or statements should include references to patent use codes, if applicable.
- Ensure all patent certifications and exclusivity statements are congruent among themselves and with the proposed labeling.

Challenge Question #2

Is the following patent certification acceptable?

[Firm] previously submitted a Paragraph IV Certification pursuant to 21 CFR 314.94(a)(12)(i)(A)(4) with respect to patent 1234567. [Firm] hereby states that we intend to extend its Paragraph IV certification to the newly listed patent use code, U-1234.

A. Yes

B. No

Electronic Labeling

Electronic Medication Guides

- Medication Guides may be distributed to authorized dispensers through a website.
  - Website must be non-promotional
  - Website should display a PDF of the Medication Guide
  - Applicants remain responsible for fulfilling its obligations under 21 CFR 208.24(b)(2) to produce Medication Guides in sufficient numbers
- May be submitted as a CBE supplement, if this is the only change to the labeling components.

Electronic Medication Guides

- Add a statement to the immediate container label and carton identifying the website for the electronic Medication Guide, such as:
  - "Dispense with Medication Guide available at: www.companyname/medguide/drugname.com."
  - "Dispense the Medication Guide provided separately to each patient." on the principal display panel (PDP) and the URL on the side panel.
- Ensure that the link(s) and/or QR codes are correctly listed and operational.
- Do not add a Medication Guide dispensing statement to the Prescribing Information or to the Medication Guide.

Electronic Prescribing Information

- **Acceptable** to provide the Prescribing Information in an electronic format in addition to providing it in a printed copy in accordance with FDA's regulations.
- Proposing to discontinue printing the Prescribing Information and substitute a website URL in its place is **not acceptable**.
  - Under 21 CFR 201.100(d), prescription drug labeling must contain the prescribing information required, and in the format specified, by 21 CFR 201.56, 201.57, and 201.80.

Other Electronic Patient Labeling

- **Acceptable** to put a URL or QR code to distribute electronic labeling on the container and carton labeling in addition to providing a physical copy of labeling.
- Proposing to discontinue printing the patient labeling, such as the Patient Information Leaflet, and substitute a website URL in its place is **not acceptable**.
  - Under 21 CFR 201.57(c)(18), patient labeling must be printed immediately following the Prescribing Information or otherwise accompany the drug product.

Challenge Question #3

The proposal to distribute an electronic Medication Guide via the addition of a URL to the container and carton labeling with no other changes may be submitted as a/n:

A. Annual report

B. Changes being effected supplement

C. Prior approval supplement

Resources

- Drugs@FDA
- Revising ANDA Labeling Following Revision of the RLD Labeling
- Updating ANDA Labeling after the Marketing Application for the Reference Listed Drug has been Withdrawn
- ANDA Submissions — Amendments to Abbreviated New Drug Applications Under GDUFA
- ANDA Submissions – Amendments and Requests for Final Approval to Tentatively Approved ANDAs
- Changes to an Approved NDA or ANDA
- Orange Book
- Medication Guides — Distribution Requirements and Inclusion in Risk Evaluation and Mitigation Strategies (REMS)

Summary

- Update generic drug labeling at the earliest time possible after FDA has approved labeling for the corresponding RLD.
- All newly listed, timely filed patent use codes must be addressed when added to an existing patent.
- It is acceptable to distribute electronic Medication Guides to a dispenser via a URL or QR code in lieu of printing physical copies.

Closing Thought

Adherence to ANDA labeling best practices facilitates the labeling review process and enables the fulfillment of GDUFA III labeling commitments – resulting in the approval of safe and effective generic drugs for the American public.

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Thank you!

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