Guidance for Industry

Revising ANDA Labeling Following Revision of the RLD Labeling

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2000
OGD

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Additional copies are available from:

Office of Training and Communications
Division of Communications Management
Drug Information Branch, HFD-210
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573

(Internet) http://www.fda.gov/cder/guidance/index.htm

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I. INTRODUCTION

This guidance is intended to assist sponsors of abbreviated new drug applications (ANDAs) in deciding when and how to submit labeling supplements following labeling revisions to their reference listed drugs (RLDs).

II. BACKGROUND

During the marketing life of a drug product approved under a new drug application (NDA), the package insert labeling is frequently revised. When an NDA serves as an RLD for an ANDA, approved changes in the RLD labeling generally necessitate changes in the labeling of one or more ANDAs using the RLD. Under the Federal Food, Drug, and Cosmetic Act and Agency regulations, an ANDA product must have the same labeling as the RLD. Section 505(j)(2)(A)(v) of the Act states that an abbreviated application for a new drug must contain

> information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug…except for changes required because of differences approved under a petition…or because the new drug and the listed drug are produced or distributed by different manufacturers.

Similar statements are also found in the regulations at 21 CFR 314.94(a)(8)(iv).

Previously, OGD notified the appropriate ANDA sponsors when the approved labeling of their RLD changed. This was usually done using a formal supplement request letter. In cases where an NDA served as the RLD for multiple generic products, the preparation of

[1]This guidance has been prepared by the Office of Generic Drugs in the Office of Pharmaceutical Science, Center for Drug Evaluation and Research (CDER), at the Food and Drug Administration. This guidance document represents the Agency's current thinking on changes in labeling of approved abbreviated new drug applications (ANDAs) following revisions in the RLD's labeling. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations, or both.

a large number of request letters took a significant amount of review staff time. With the increase in the numbers of approved NDAs and ANDAs, this approach was using an increasingly disproportionate share of OGD's resources. Because of the time it took, the approach sometimes even delayed the notification of ANDA sponsors. With the exception of a few special situations (noted below), ***OGD is no longer providing this type of notification***. The sponsor of an ANDA is now responsible for ensuring that the labeling contained in its application is *the same as* the currently approved labeling of the RLD. OGD has determined that this change in responsibility is necessary to minimize the implementation time for the introduction of revised labeling into the market place. OGD believes that prompt revision, submission to the Agency, and implementation of revised labeling are important to ensure the continued safe and effective use of generic drug products. Because the regulations state that the labeling of the generic must be the same as the innovator, the revision should be made at the very earliest time possible. If there is any potential delay in the revision of a generic drug labeling, the sponsor should contact OGD.

III. HOW TO OBTAIN INFORMATION ON A CHANGE IN RLD LABELING

The sponsor of an ANDA should routinely monitor the Labeling Review Branch Homepage (see below) for information on changes in labeling. OGD's Labeling Review Branch will:

- Place monthly updates of approved labeling changes for RLDs with approved ANDAs on the Labeling Review Branch Homepage at:

  http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

Continue to notify ANDA applicants by facsimile, telephone, and/or letter for any labeling revision approved for the RLD that warrants ***immediate*** widespread professional notification, such as those changes connected to issuing a *Dear Doctor Letter* or similar significant changes.

All approved labeling for RLDs is still available from Freedom of Information Staff. Sponsors who wish to obtain labeling using this mechanism should send a written or facsimile request to:

Food and Drug Administration
Freedom of Information Staff (HFI-35)
5600 Fishers Lane
Rockville, MD 20857
Phone: 301-827-6500; FAX: 301-443-1726

When a labeling revision is needed, the ANDA sponsor should take appropriate action to revise the ANDA labeling and submit the revised labeling to the FDA.

IV. HOW TO SUBMIT REVISED LABELING

All ANDA labeling changes needed because of approved changes to the labeling of the RLD may be submitted as a *Special Supplement – Changes Being Effected*. Such supplements should include:

- 12 copies of final printed labeling
- the date the revised labeling will be used (go into effect)
- a side-by-side comparison of the ANDA labeling with the approved labeling of the RLD with all differences annotated and explained, as described in 21 CFR 314.94 (a)(8)(iv)

Sponsors should contact the OGD Labeling Review Branch at 301-827-5846 if there are any questions about the information in this guidance.