OFFICE OF GENERIC DRUGS

Review of Generic Drug Product Labeling Requiring Input From Multiple FDA Components

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PURPOSE

- This MAPP outlines procedures for the review of generic drug product labeling that requires input from multiple FDA components in addition to the Office of Generic Drugs (OGD). Frequently, this need is related to provisions of Section 11 of the Best Pharmaceuticals for Children Act (BPCA), but the general procedures are applicable to other labeling issues.

BACKGROUND

- Historically, when clinical or legal questions were presented in the review of package insert labeling for generic drug products, OGD labeling reviewers have sent a consult to the appropriate Office of New Drugs (OND) clinical review division or to the Office of the Chief Counsel (OCC) to evaluate proposals from the sponsor of the abbreviated new drug application (ANDA). Recently, issues have become more complex, often necessitating review of the labeling by multiple FDA components outside OGD. Issues can include those related to the BPCA (see below), patents and exclusivity, or other components of labeling such as trade names, Medication Guides, patient package inserts (PPIs), and risk management programs. These issues must be addressed to develop the best product labeling within the limits of the Federal Food, Drug, and Cosmetic Act.

- On January 4, 2002, the President signed the BPCA into law. This act contains a number of provisions to encourage the development of medications for use in pediatric patients. Section 11 of the BPCA addresses the issue of an innovator gaining approval of labeling with pediatric information that qualified for 3-year Hatch-Waxman exclusivity that could potentially block the approval of a generic product. Section 11 allows generic applications to be approved with labeling specifying that the generic product is not indicated for use in pediatric patients and

refers the practitioner to the innovator product approved for use in pediatric patients. It also allows for the inclusion of certain warnings or precautions from the protected labeling that are deemed critical to create a safe label for the generic product.

- To ensure that only labeling providing information for safe use of generic drug products is approved, it may be necessary to consult OND, the Office of Counter-Terrorism and Pediatric Drug Development (OCTPDD), OCC, the Office of Drug Safety (ODS), and/or other FDA components. This document describes the process by which the necessary reviews will be obtained by the Office of Generic Drugs.

REFERENCES

- Federal Food, Drug, and Cosmetic Act (Public Law 75-717)
- Best Pharmaceuticals for Children Act (Public Law 107-109)
- 21 CFR 314.94 (a)(8)

POLICY

- The Office of Generic Drugs will obtain necessary input from the Office of New Drugs, Office of Counter-Terrorism and Pediatric Drug Development, the Office of Drug Safety, and/or other appropriate FDA components in a manner that allows optimum input from all components.
- In many instances (particularly if the labeling is under the BPCA), labeling will be sent to the Office of the Chief Counsel (OCC) to ensure that it is in accord with all applicable laws and regulations and is consistent with any related legal opinion.

RESPONSIBILITIES AND PROCEDURES

The OGD Labeling Reviewer will:

- Complete the standard review of the draft generic product labeling submitted by the ANDA sponsor
- Promptly identify issues that require input from other FDA components
- Ensure that appropriate changes are made to the generic drug product labeling when the innovator has Hatch-Waxman exclusivity and Section 11 of the BPCA applies. Generally, that labeling will need to contain a statement consistent with Section 11 of the BPCA (i.e., “Pediatric usage information for [established name] is approved for [reference listed drug holder’s][drug product name]. However, due to [reference listed drug holder’s] marketing exclusivity rights, this drug product is not labeled for pediatric use”).

- Make an initial determination as to what pediatric contraindications, warnings, precautions, or other information should remain in the labeling for safety reasons.

- Prepare and send consults to the appropriate FDA components. The consults should clearly state the questions and/or requested action. Typically, if OND input is needed, consults should be sent to the clinical review division first. A side-by-side draft of the approved reference listed drug labeling and the proposed labeling should be prepared so that the clinician can see both the original text and all proposed changes. Contraindications, warnings, or precautions being retained in the proposed generic labeling (even though related to pediatric use of the product) should be highlighted. A rationale must be provided indicating why the labeling reviewer believes the statements should remain in the label.

- Send the agreed upon-labeling to OCTPDD, ODS (for trade names, PPIs, Medication Guides, risk management programs), or appropriate review groups (other than OCC) after the consult is returned from the OND division. Changes requested by the new drug reviewer will be clearly marked for evaluation by the OCTPDD reviewer.

- Provide the resulting labeling to the sponsor, if appropriate, after comments are received from OND, OCTPDD, ODS, or other groups, and after any discrepancies in review recommendations are resolved. If there are discrepancies in review recommendations that cannot be resolved by e-mail, they may need to be resolved in a meeting of all reviewers.

- Discuss with appropriate OGD staff whether labeling should be sent to OCC for review. OGD staff consulted often will include Special Assistants and the Director of OGD. Consults to OCC should clearly indicate what other components (i.e., OND, OCTPDD, ODS) have reviewed the labeling, and should show concurrence and any recommendations by those groups. Consults to OCC should be directed through a Special Assistant in the OGD Immediate Office so that an OCC Tracking Form (COMIS form) can be generated and signed by the Director of OGD.

- Present the agreed upon mock-up labeling to OCC in a side-by-side comparison with the currently approved reference listed drug labeling. This will usually require that the labeling reviewer generate the mock-up rather than relying on the firm to provide it.

- When a meeting is necessary, send the mock-up labeling compared side-by-side to the reference labeling to all proposed attendees in ample time for review. Questions to be resolved in the meeting must be stated and must accompany the labeling. If OCC is to attend the meeting, a COMIS form may also be necessary.

- Send the final labeling recommendations to the ANDA holders for incorporation into their final printed labeling (FPL). If there are multiple applications for a particular product, the recommendations will be provided at the same time, but in a manner that preserves confidentiality for each applicant.

- Review the revised FPL according to OGD's first-in, first-reviewed policy and, if acceptable, prepare a labeling approval summary.

EFFECTIVE DATE

- This MAPP is effective upon date of publication.