OFFICE OF ESTABLISHMENT LICENSING AND PRODUCT SURVEILLANCE
ADVERTISING AND PROMOTIONAL LABELING STAFF

Procedural Guidance Document

DRAFT

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This document has been revised to address comments received subsequent to the announcement of availability in the Federal Register dated August 9, 1993. This document replaces the previous edition dated July 1993.

THE ADVERTISING AND PROMOTIONAL LABELING STAFF PROCEDURAL GUIDE

Introduction

This guidance document was developed to assist manufacturers in understanding the current procedures to be followed for the submission of promotional labeling and advertising materials to the Center for Biologics Evaluation and Research. FDA is currently reviewing its regulation on guidelines in 21 CFR 10.90(b), and therefore, this document is not issued under this regulation.

As with other guidance documents, FDA does not view this document as all inclusive, and recognizes that alternative approaches may be suitable in specific situations. This document does not bind FDA and does not create or confer any rights, privileges, or benefits on or for any person, and is intended merely for guidance.

Procedure

In an effort to reduce the burden of reporting, the Center for Biologics Evaluation and Research (CBER) is providing guidance on its current interpretation of the regulation for reporting important proposed changes in the labeling of biologic products, as applicable to promotional labeling [see 21 CFR 601.12]. This document does not change the procedures to be followed for the submission of changes to container or package labels, and circulars (package inserts). Labeling (which includes promotional labeling) is defined in section 201(m) of the Act, promotional labeling is described in 21 CFR 202.1(l)(2) and is subject to various provisions in the Act including sections 502(a) and (f). Examples of advertisements subject to section 502(n) of the Federal Food, Drug and Cosmetic Act are described in 21 CFR 202.1(l)(1) of the regulations.

For promotional labeling, CBER has determined that preapproval is required only for any biological product for which a license is pending, for "newly approved" products (the first 120 days following approval), and any licensed biological products for which a supplement has been filed that requests or would require a labeling change. Supplements requiring a change in the labeling include new indications for use, new dosage forms or dosing regimens, expanded patient population and additional safety or effectiveness information.

Manufacturers of biological products reviewed under the Accelerated Approval regulations [Reference 21 CFR 601 Subpart E] must continue to submit, after the 120 days following approval, all promotional materials, including promotional labeling and advertising, at least 30

days prior to the intended time of distribution and/or dissemination, until otherwise notified by this Center.

For introductory advertising materials, it is requested that manufacturers continue to submit before publication/dissemination, for review only, proposed drafts of introductory advertising materials including "Coming Soon" advertisements, launch advertisements and those advertisements intended to be used in the first 120 days following approval.

CBER will review all advertising and promotional labeling for products that have been licensed for more than 120 days on a surveillance basis (except as noted above for products reviewed under the Accelerated Approval regulations).

The FDA form 2567 is to be used for all introductory advertising and promotional labeling, all materials following approval, as well as any submission for a request for review and comment. Applicants should submit all proposed drafts of introductory advertising and promotional labeling, including all "Coming Soon" pieces and "launch" materials in duplicate with Part I of the form FDA-2567, to the Advertising and Promotional Labeling Staff (APLS) prior to the issuance of a biological product license and/or receipt of an approval letter.

Applicants may request the APLS to review and comment on a proposed promotional labeling piece or an advertising campaign at any time. This request should be in writing, accompanied by Part I of the form FDA-2567 and sent directly to APLS.

Applicants should continue to submit to APLS final copies of all advertising and promotional labeling with Part II of the form FDA-2567, at the time of initial publication of the advertisement or distribution of the promotional labeling, for inclusion in their product files.

Part II of the completed form FDA-2567 should accompany all final printed, published or produced material and all media.

Please follow the instructions provided below in completing the form FDA-2567:

1. The form should be typed.

2. Include the license number and name of the firm in the space provided for the manufacturer's name.

   If a license is pending and has not been issued, or if the submission reflects information contained in a supplement to an existing Product License Application, include the reference number of the pending submission.

3. The form should be signed by the responsible head with the typed name also appearing (signatures are often difficult to read).

4. List the in-house control number and revision date for each piece.

5. To minimize delays, we suggest using one completed form per piece to be reviewed. This will enable APLS to process through ("clear") the material found to have no objection for use. However, similar and closely related materials may be submitted on one form.

6. If the material was previously reviewed by us, include the label review number previously assigned to the piece in the appropriate space on the form.

Prior to dissemination of introductory or launch promotional labeling, manufacturers need to obtain APLS review and approval. Advertisements for use in launch campaigns will be reviewed for consistency against other launch materials to be used in the first 120 day period.

All advertising materials and promotional labeling for all biologic products will be monitored to determine that they:

1. are not false or misleading in any particular manner;

   For example, a sponsor cannot make claims of greater safety and or efficacy than what was demonstrated in clinical trials used to support licensure or make "global" claims of efficacy or safety on the basis of results obtained in one trial with a limited scope.

2. are consistent with the current approved labeling (package insert) or applicable sections of the FD&C Act and regulations concerning advertising and labeling, clinical trial data used to support licensure, relevant information contained in the Summary Basis of Approval (SBA) and when applicable, previously approved promotional labeling;

3. present a "fair balance" of information about the product;

   Applicants should balance claims of safety or efficacy with related information regarding any safety concerns or side effects, etc.

4. include proper prescribing information (a minimum of a "brief summary" for advertisements and full prescribing information for all promotional labeling).

   [Reference FD&C 502(a)&(f); 502(n)1,2,&3; 21 CFR 201.100(d) and 21 CFR 202.1]

The review time for introductory or launch campaigns depends directly on the scope, completeness of the submission, and the depth and expanse of the initial campaigns. APLS anticipates the average review time to be approximately four weeks from the date the material is received by the staff.

After APLS completes its review of the new promotional material , APLS will notify the manufacturer of the completion of the review by a previously agreed upon form of electronic communication and followed up with hard copy by mail. The hard copy constitutes the official acknowledgement.

If problems are discovered in the course of the review, the APLS staff may contact the Responsible Head or approved alternate Responsible Head in the event of an unavoidable absence. APLS will provide comments and requests for modifications or revisions will be in writing and noted on Part I of the form FDA 2567 unless otherwise discussed and noted. APLS will arrange meetings between the manufacturer, the CBER review division, and any other parties or disciplines involved, to resolve outstanding issues as needed.

Upon resolution of any problems encountered during the review, manufacturers should send the corrected material as final copy, in duplicate with Part II of form FDA-2567, along with a copy of the package insert to the APLS as a routine submission for record purposes.

Following the 120 day period after approval, manufacturers are requested to submit final printed copies of all advertising and promotional labeling at the time of initial publication or dissemination to allow the APLS to review the materials on a surveillance basis. As stated earlier in this document, manufacturers of those products reviewed under the Accelerated Approval regulations are required after the 120 day period following approval, to submit promotional materials at least 30 days prior to their intended distribution and/or dissemination until otherwise notified by this Center.

When manufacturers make changes to the approved package insert that affect the message in their promotional materials, manufacturers should submit proposed copies of all affected advertising and promotional labeling identifying the changes in the comment section of Part I of the form FDA 2567. Manufacturers should submit the revised package insert with the revised promotional materials. In those cases where the printing or inclusion of the full prescribing information is integrated into the promotional labeling piece, as in file cards or brochures, the material should be resubmitted as a "new" piece.

If the information or message in the promotional materials is not affected by the labeling change and the full prescribing information is included in a separate pocket or sleeve, then it is not necessary to resubmit the product promotional materials. However, it is the responsibility of the manufacturer to ensure that the previous version of the package insert (full prescribing information) has been replaced with the most recent, approved package insert prior to distribution or dissemination.

The staff may initiate regulatory action if the advertising and promotional labeling are not consistent with the approved labeling (package insert), clinical data used to approve the product, or applicable sections of the FD&C Act and regulations for labeling and advertising by notifying the manufacturer in writing of the violations. If significant problems in the advertising

or promotional labeling are discovered that could pose a potential health hazard, or if violations as cited in previous correspondence persist, a "Warning" letter may be issued. These letters will request that corrective actions be taken, including the material in question be discontinued or canceled promptly.

If further regulatory action is warranted (e.g., because of past history or if dissemination of the material poses a potential health hazard), APLS will work with the Office of Compliance to implement appropriate compliance actions as necessary.

The effective date for implementation of this revised procedure by the Advertising and Promotional Labeling Staff is July, 1994.