Guidance for Industry

Forms for Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability published in the *Federal Register*.

For questions regarding this draft document contact Kathy Smith, 301-594-1086, for drug related questions; Robert A. Yetter, 301-827-0373, for biologics related questions; and Lowell Fried, 301-827-0165, for veterinary related questions.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

April 2001
Procedural

Guidance for Industry

Forms for Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution

Additional copies are available from:

Office of Training and Communications
Division of Communications Management
Division of Drug Information HFD-240
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573
(Internet) http://www.fda.gov/cder/guidance/index.htm

or

Office of Communication, Training and
Manufacturers Assistance, HFM-40
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Rockville, MD 20852-1448
(Internet) http://www.fda.gov/cber/guidelines.htm
Fax: 1-888-CBERFAX or 301-827-3844
Phone: the Voice Information System at 800-835-4709 or 301-827-1800
or

Communications Staff (HFV-12),
Center for Veterinary Medicine (CVM)
7500 Standish Place, Rockville, MD 20855 (Tel) 301-594-1755
(Internet) http://www.fda.gov/cvm/guidance/guidance.html

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)

April 2001
Procedural

TABLE OF CONTENTS

Draft - Not for Implementation

Guidance for Industry[1]
Forms for Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. 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 and regulations.

I. INTRODUCTION

This guidance is intended to assist private label distributors and establishments, which are required to register ("registrants") and list drugs and biological products, in obtaining and submitting the necessary forms to meet the registration and listing requirements set forth at 21 CFR part 207, as authorized or required under section 510 of the Federal Food, Drug, and Cosmetic Act ("the Act") and sections 351 and 361 of the Public Health Service Act. To the extent that information provided in this draft guidance differs from previously disseminated information (e.g. certain information in the Drug Registration and Listing Instruction Booklet), this guidance will supersede any such information when finalized.

FDA is developing software to make possible the electronic submission of the requisite registration and listing information for drugs and biological products. While this software is being developed, FDA will make establishment registration and listing forms available on the Internet. Since FDA will provide these forms via the Internet, FDA will no longer provide registrants with annual re-registration forms via conventional mail, unless specifically requested. Internet availability of these forms (instead of by conventional mail), until an electronic submission system is fully implemented, is part of an Agency initiative to use modern technology to facilitate the submission of establishment registration and listing information. The Agency plans to propose rulemaking that would revise the requirements on registration and listing, and would require registrants to submit this information electronically.

II. BACKGROUND

Section 510 of the Act and 21 CFR part 207, inter alia, require establishments (e.g. manufacturers, repackers, and relabelers) upon first engaging in the manufacture, preparation, propagation,

[1] The Office of Compliance and the Office of Information Technology in the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Review prepared this guidance.

compounding, or processing of human drugs, veterinary drugs, and biological products, with certain exceptions, to register their establishments and submit listing information for all drugs and biological products in commercial distribution. Registrants are also required to submit, on or before December 31 of each year, updates in registration information for their establishments.[2] Registrants must, at the time of annual registration, also submit required listing information. Additionally, registrants are required to update listing information every June and December of each year to include information for drugs and biological products that have not been previously listed. Certain changes to information for previously listed drugs and biological products must also be submitted every June and December of each year.

Under section 351(j) of the Public Health Service Act (PHS Act), the Act and regulations promulgated under the Act apply to biological products. In addition, section 361 of the PHS Act authorizes FDA to promulgate regulations to prevent the introduction, transmission, and spread of communicable disease. Under this authority, FDA promulgated 21 CFR 207.20(f), which requires manufacturers of those human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulated as drugs and/or biological products under the Act and section 351 of the PHS Act to register and list their HCT/Ps using new Form FDA 3356 beginning January 21, 2003.

III. REGISTRATION AND LISTING FORMS

Various forms have been used to collect registration and listing information. In the past, FDA mailed these forms for industry to complete or, in some cases, verify the information and return. However, these forms are now easily accessible on the Internet. Since the distribution of these forms through the mail is burdensome and time-consuming, the Agency is discontinuing the conventional mailing of the following registration and listing forms:

A. Form FDA 2656 (Registration of Drug Establishment/Labeler Code Assignment)

Since FDA will provide forms via the Internet, FDA will no longer provide annual re-registration forms via conventional mail, unless specifically requested. If registrants would like to receive annual re-registration forms via conventional mail, registrants may direct such requests to the agency contacts designated in this guidance. Additionally, annual re-registration and changes to registration information that, in the past, were reported on Form FDA 2656e should now be reported on Form FDA 2656, in accordance with current regulations. Registrants should review their previous Forms FDA 2656e submitted to the Agency for information reported and contained in FDA's database. If registrants have questions regarding previously submitted information, they should direct inquiries to the appropriate contacts designated elsewhere in this draft guidance document.

Form FDA 2656 is used by:

[2] Failure to register in accordance with section 510 of the Act is a prohibited act under section 301(p) of the Act. Failure to comply with section 510 of the Act renders drugs misbranded under section 502(o) of the Act.

- Manufacturers, repackers, and relabelers registering an establishment with FDA for the first time. The form must be submitted within 5 days after beginning the manufacture or processing (which includes, inter alia, repackaging and relabeling) of drugs and biological products; alternatively, if the establishment has not previously entered into such an operation, the establishment must register within 5 days after submitting a drug application or biological license application. See 21 CFR 207.21(a).

- Medicated feed mill establishments. Registration must be obtained prior to approval of a medicated feed mill license application. See 21 CFR 515.10.

- Private label distributors obtaining a labeler code.

- Manufacturers, repackers, relabelers, and private label distributors reporting changes in registration information or labeler code information.

B. Form FDA 2657 (Drug Product Listing)

Form FDA 2657 is used by:

- Registrants reporting the initial listing information for all drugs and biological products in commercial distribution. This form must be submitted within 5 days of beginning the manufacturing or processing of drugs and biological products. See 21 CFR 207.21(a) and 21 CFR 207.22(b).

- Private label distributors that elect to submit listing information directly to FDA.

- Registrants and private label distributors updating listing information for drugs and biological products that have subsequently been introduced for commercial distribution and, therefore, have not previously been listed. This form is also used to report certain changes to information for previously listed drugs and biological products. Any updates must be submitted every June and December or, at the discretion of the registrant, when any change occurs. See 21 CFR 207.21(b), 21 CFR 207.22(b), and 21 CFR 207.30.

C. Form FDA 2658 (Registered Establishments' Report of Private Label Distributors)

Form FDA 2658 is used by:

- Registrants reporting listing information for those private label distributors that do not elect to submit listing information directly to FDA.

- Registrants updating listing information for private label distributors. This information must be submitted every June and December or, at the discretion of the registrant, when any change occurs. See 21 CFR 207.20(b) and 21 CFR 207.30.

IV. INFORMATION UPDATES

A. How to Update Registration Information

Forms FDA 2656, 2657, and 2658 are available on the Internet at www.fda.gov/cder/drls/registration_listing.htm.

1. To submit annual re-registration information and to report any changes, registrants should complete the following fields on Form FDA 2656:

- Labeler Code
- Registration Number
- Reporting Firm Name
- Reason(s) for Submission (write in "ANNUAL")
- Section D (signature, title, and, date)
- Other sections of the form where changes have occurred

Registrants should **not** complete any other sections where information has remained the same.

2. If there are no changes to report, the following fields should be completed on Form FDA 2656:

- Labeler Code
- Registration Number
- Reporting Firm Name
- Reason(s) for Submission (write in "ANNUAL – NO CHANGE")
- Section D (signature, title, and date)

No other section of the form should be completed.

The Agency encourages submission of annual updates according to the schedule outlined in the current regulations (21 CFR 207.21(a)). However, annual re-registration information must be submitted on or before December 31 of each year, as required by section 510 of the Act.

It should be noted that since FDA is providing forms via the Internet, FDA will no longer provide registrants with annual re-registration forms via conventional mail, unless specifically requested. If registrants would like to receive annual re-registration forms via conventional mail, or they are unable to download the forms from the Internet, the forms can be obtained by requesting them from the Office of Training and Communications, Division of Drug Information,

HFD-240, 5600 Fishers Lane, rm. 12B31, Rockville, MD 20855, (Tel) 301-827-4573. A request for a form using the mail or telephone may take up to 14 days to process. The Agency encourages downloading forms from the Internet, at the Internet address above, to expedite the process.

B. How to Update Product Listing Information

In addition to the forms discussed above, in the past, FDA has periodically mailed to drug establishments a Compliance Verification Report, which is a printout of information from the registrant's listing information previously reported to FDA on Form FDA 2657 or Form FDA 2658. The Agency requested that companies verify or correct the information in the report and return it to the Agency within 30 calendar days of receipt. The Agency considered verification of this information to satisfy the June listing requirement for prescription products.

FDA is discontinuing the mailing of the Compliance Verification Report. After submitting initial drug listing information, registrants and, if applicable, private label distributors must update their listing information by using Form FDA 2657 and/or Form FDA 2658, every June and December, or at the discretion of the registrant, when any change occurs, in accordance with section 510 of the Act and 21 CFR part 207. We recommend submitting forms as soon as possible once a change occurs so that the information can be correctly reflected in *the National Drug Code Directory*.

To report any changes to listing information, registrants and private label distributors should complete the following fields on Form FDA 2657:

- Name and Address of Firm
- Product Trade Name
- National Drug Code (Labeler, Product, Package)
- Other sections of the form where changes have occurred

To report any changes to listing information, registrants should complete the following fields on Form FDA 2658:

- Reporting Firm Name
- Reporting Firm NDC Code (Labeler, Product, Package)
- Other sections of the form where changes have occurred

Registrants and private label distributors can consult the *National Drug Code Directory* for a listing of all human prescription drug products listed with the Agency. If a human prescription drug product does not appear in the directory, then FDA will not consider it listed with the Agency. For a product to be listed by the Agency, the company must provide complete and accurate information on the Form FDA 2657 or Form FDA 2658. This directory is available on the Internet at http://www.fda.gov/cder/ndc/index.htm.

V. SUBMISSION OF FORMS

Completed forms 2657 and 2658 for veterinary drugs submitted by mail should continue to go to CVM/OSC/OS/MPIT, HFV-212, 5700 Standish Place, rm. 446, Rockville, MD 20855. All other completed forms submitted by mail should continue to be sent to the Food and Drug Administration, CDER/Drug Registration & Listing, HFD-330, 5600 Fishers Lane, Rockville, MD 20857.

Completed forms FDA 2657 and 2658 for veterinary drugs may be hand carried to CVM/DCU, HFV-199, 7500 Standish Place, rm. N403, Rockville, MD 20855. For all other forms that are being hand carried, they should be delivered to Food and Drug Administration, CDER/Drug Registration & Listing, HFD-330, 5901-B Ammendale Rd, Beltsville, MD 20705.

VI. HUMAN CELLS, TISSUES, AND CELLULAR AND TISSUE-BASED PRODUCTS -- ESTABLISHMENT REGISTRATION AND LISTING

On January 19, 2001, FDA promulgated 21 CFR 207.20(f), which requires establishments that manufacture those human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulated as drugs and/or biological products under the Act and § 351 of the PHS Act to register and list their HCT/Ps using new Form FDA 3356 beginning January 21, 2003 (66 FR 5447, January 19, 2001). Until then, such establishments should continue to register and list using the forms and procedures provided in part 207, as discussed above.