

Preparing for Mandatory Electronic Submission of Drug Establishment Registration and Drug Listing Information

Prepared by

Gina A. Ross
Greg A. Onyszchuk, Ph.D.

Beckloff Associates, Inc.

Introduction

United States federal laws make mandatory the registration of drug establishments, including both domestic and foreign, and the submission of drug listing information to FDA^{1,2,3}.

Effective June 1, 2009, there are important changes to the requirements – and these changes apply to every company that has a drug establishment registration or drug listing with FDA⁴.

Your immediate action is required.

What is New?

The submission of establishment registration and drug listing forms has been completed exclusively on paper until recently. The Food and Drug Administration Amendments Act (FDAAA), which was signed into law on September 27, 2007, requires that drug establishment registration and drug listing information be submitted electronically.

FDA Guidance to Industry – *Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing*, dated July 2008 describes that beginning June 1, 2009, drug establishment registration and drug listing information must be submitted in electronic format only.

Electronic Format and Electronic Submission

The guidance indicates that beginning June 1, 2009, electronic format *and* electronic submission via the FDA Electronic Submissions Gateway (ESG) will both be required. The FDA ESG is FDA's centralized agency-wide system for receiving electronic regulatory submissions. Paper submissions, and submissions sent on physical media will not be accepted.

FDA Forms 2656, 2657, and 2658

The following paper forms are the instruments that have been used for accomplishing drug establishment registration and for providing drug listing information to FDA:

Form FDA 2656 – Registration of Drug Establishment/Labeler Code Assignment

Form FDA 2657 – Drug Product Listing

Form FDA 2658 – Registered Establishment’s Report of Private Label Distributors

According to the guidance, the information previously provided on these paper forms should be provided via electronic means beginning June 1, 2009.

Which Companies are Required to Register and/or Submit?

A list of the types of firms required to register establishments and/or submit drug listing information is found on the FDA CDER Drug Registration and Listing Instructions web page (electronic reference provided below), and includes manufacturers, contract manufacturers, label repackagers, relabelers, contract testing labs, contract sterilizers, fulfillment packagers, active drug substance manufacturers, foreign drug manufacturers, manufacturing pharmacies and others.

How Frequently are Registrations and Submissions Required?

Federal laws require an initial drug establishment registration to be followed by an annual update (re-registration) before December 31 of every calendar year. Drug listing submissions are required at the time of drug establishment registration, followed by updates twice annually in June and December.

Why Electronic Submission?

The volume of information related to drug establishments and drug listings is substantial. In 2006, the FDA regulated more than 375,000 establishments in approximately 100 countries⁵.

In support of the FDA mission to protect the public health, electronic registration and drug listing submission is intended to improve the timeliness and accuracy of the information received, and to support a more effective and efficient automated agency process. The guidance indicates that a properly created and complete electronic file “can be processed in minutes”.

What is the Electronic Format?

The FDA is calling for drug establishment registrations and drug listing submissions to be prepared in extensible markup language (XML) files in the Structured Product

Labeling (SPL) format. SPL has been the required format, since October 2005, for the submission of the content of labeling associated with NDAs, ANDAs, and BLAs.

FDA expects drug establishment registration and drug listing submissions to be made using SPL-R4, the latest release of SPL that includes enhanced capabilities for interfacing with the FDA's electronic drug listing system - eLIST. SPL-R4 files are typically prepared using specialized software with XML authoring and SPL-R4 capabilities.

Is the June 1, 2009 Deadline Firm? What About Waivers?

The guidance for electronic drug establishment registration and drug listing is very clear in stating that, unless a waiver is granted, FDA "expects to receive all drug establishment registration and drug listing information in electronic format". The guidance further clarifies that FDA "does not anticipate the need to grant many waivers".

Recommended Immediate Course of Action

Businesses that are required to register (and re-register annually) their drug establishments, and those who are required to submit drug listing information (and submit updates twice annually), should have a solution in place by June 1, 2009, for the preparation of this required information in SPL-R4 format files, and for the submission of these files through the FDA ESG.

Consider Expert Assistance

If your organization does not currently have or expect to have these elements in place by or before June 1, 2009, you may consider using an appropriately-equipped regulatory publishing service provider or outsourcing partner to prepare the information for you.

Call Beckloff Associates for Help

As an outsourcing partner that has published extensively in electronic formats, has experience with SPL, has a validated process for submission of documents through the ESG, and has experience interpreting appropriate regulatory guidances, Beckloff Associates is ideally positioned to assist you.

Our service solution, including the preparation of the electronic files, and the secure transmission of these through the FDA ESG, will meet your needs from June 1, 2009.

To obtain more information, or to arrange for preparation and submission of electronic Drug Establishment Registration or Drug Listing Information, please contact Beckloff Associates at: **913.451.3955**, or send an e-mail to **info@beckloff.com**, or visit our web pages at www.beckloff.com.

References:

1. FDA CDER web page for Drug Registration and Listing Instructions (Section 510 of the Federal Food, Drug, and Cosmetic Act, in section 351 of the Public Health Service Act): www.fda.gov/cder/drls/
2. FDA CDER web page for the Division of Compliance Risk Management and Surveillance (Title 21 of the Code of Federal Regulations (21 CFR Part 207)): www.fda.gov/cder/Offices/CRMS/DRLS.htm
3. Final Rule in Federal Register Notice, requiring foreign drug establishments to register with the FDA and identify a U.S. agent (Federal Register Notice of November 27, 2001 and became effective May 24, 2002): www.fda.gov/ohrms/dockets/98fr/112701a.htm
4. Guidance for Industry – *Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing*:
www.fda.gov/cder/guidance/OC2008145.htm
[www.fda.gov/cder/guidance/OC2008145\(2\).pdf](http://www.fda.gov/cder/guidance/OC2008145(2).pdf)
5. FDA Science and Mission at Risk: Report of the Subcommittee on Science and Technology, providing statistics on FDA’s responsibilities, costs and activities: www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf

Additional Useful References:

Structured Product Labeling Implementation Guide for FDA Drug Establishment Registration and Drug Listing:

www.fda.gov/oc/datacouncil/SPL_r4_IG_v1.0.pdf

Guidance for Industry - *Providing Regulatory Submissions in Electronic Format – Content of Labeling*: www.fda.gov/cder/guidance/6719fnl.pdf

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