Guidance for Industry

Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing

U.S. Department of Health and Human Services
Food and Drug Administration
Office of the Commissioner

May 2009
Electronic Submission

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Contains Nonbinding Recommendations

Guidance for Industry

Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing

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Center for Drug Evaluation and Research
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5600 Fishers Lane
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Food and Drug Administration
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Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing

This guidance represents 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. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This is one in a series of guidance documents intended to assist persons making regulatory submissions to FDA in electronic format. This guidance is designed to assist manufacturers with electronic submissions of drug establishment registration and drug listing information. The guidance and accompanying technical documents explain (among other things):

- The statutory requirement to submit electronically drug establishment registration and drug listing information;
- How to create a Structured Product Labeling (SPL)[2] file for submitting drug establishment registration and drug listing information to FDA through the Electronic Submissions Gateway (ESG) using defined code sets and codes, i.e., a language recognized by the computer system; and
- Beginning June 1, 2009, FDA intends to no longer accept drug establishment registration and drug listing information in paper format unless a waiver is granted.

FDA intends to update these documents regularly to reflect the evolving technology and user experience.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

[1] The Office of Critical Path Programs, Office of the Commissioner, Food and Drug Administration prepared this guidance document in cooperation with the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Veterinary Medicine.

[2] SPL standard is a Health Level Seven, Inc. standard for the exchange of product information using extensible markup language (XML).

Requirements for drug establishment registration and drug listing are set forth in section 510 of the Federal Food, Drug, and Cosmetic Act (the Act) and section 351 of the Public Health Service Act (the PHS Act), and 21 CFR Part 207.[3] Fundamental to FDA's mission to protect the public health is the collection of this information, which is used for important activities such as postmarket surveillance for serious adverse drug reactions, inspection of drug manufacturing and processing facilities, and monitoring of drug products imported into the United States. Comprehensive, accurate, and up-to-date information is critical to conducting these activities with efficiency and effectiveness.

Section 510 of the Act and 21 CFR part 207, subject to certain limited exceptions, require establishment owners and operators (registrants) upon first engaging in the manufacture, preparation, propagation, compounding, or processing of drugs, (including human drugs, veterinary drugs, and biological drug products[4]) to register their establishments and submit listing information for all drugs in commercial distribution. Registrants are also required to submit registration information for their establishments on or before December 31 of each year.[5] At the time of registration, registrants must also submit required listing information.[6] Additionally, registrants are required to update listing information in June and December of each year to include information for drugs that have not been previously listed.[7] Certain changes to information for previously listed drugs must also be submitted every June and December.[8]

Changes in the Act, resulting from the Food and Drug Administration Amendments Act of 2007 (Public Law 110-85) (FDAAA),[9] require that drug establishment registration and drug listing information be submitted electronically unless a waiver is granted. Before FDAAA was enacted, section 510(p) of the Act expressly provided that drug establishment registration information must be submitted electronically, based on a finding that electronic receipt was feasible, and section 510(j) of the Act stipulated that drug listing information must be submitted in the form and manner prescribed by FDA. Section 224 of FDAAA, which amends section 510(p) of the Act, now expressly requires drug listing information to be submitted by electronic means in addition to requiring electronic drug establishment registration.

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[3] This guidance document does not apply to establishment registration and product listing information required solely under 21 CFR part 607 (Blood and Blood Products), 21 CFR part 807 (Devices), and 21 CFR part 1271 (Human Cells, Tissues, and Cellular and Tissue-Based Products).

[4] Under section 351(j) of the PHS Act, the Federal Food, Drug, and Cosmetic Act (and regulations promulgated thereunder) applies to biological drug products, except that New Drug Applications (NDAs) are not required for products licensed under section 351(a) of the PHS Act.

[5] Section 510(b)(1) of the Act.

[6] Section 510(j)(1) of the Act.

[7] Section 510(j)(2)(A) of the Act.

[8] Section 510(j)(2) of the Act.

[9] Signed into law on September 27, 2007.

Drug establishment registration and drug listing information have, until now, been submitted using a paper-based format, i.e., Form FDA 2656 (Registration of Drug Establishment/Labeler Code Assignment), Form FDA 2657 (Drug Product Listing), and Form FDA 2658 (Registered Establishments' Report of Private Label Distributors).[10] Moving from a paper-based format to an electronic system will improve the timeliness and accuracy of the submissions.

Prior to the amendment of the statute to require electronic submission of both drug listing and establishment registration information, FDA issued a proposed rule that would amend 21 CFR part 207 to require electronic submission of drug establishment registration and drug listing information, and that included proposals such as certain changes to the National Drug Code (NDC) system and requirements regarding placement of the appropriate NDC on the drug label (71 FR 51276, August 29, 2006). FDA is considering comments submitted on the proposed rule and intends to issue a final rule based on that proposal which will also serve to conform the regulations to the changes in section 510(p) mandating electronic submission. FDA intends to revise, reissue, or revoke this guidance document as appropriate to make it consistent with the final rule, when the rule is issued.

To facilitate the submission of drug establishment registration and drug listing information (including labeling as specified under 21 CFR 207.25), FDA is adopting the use of extensible markup language (XML) files in a standard SPL format. The automated submission process functions most efficiently and effectively when this information is provided in a standardized format with defined code sets and codes. This guidance and accompanying technical documents describe how to make these submissions using the SPL format, which FDA can process, review, and archive.[11] Information in a properly created and complete SPL file can facilitate processing and allows for greater precision and accuracy through the use of coded data fields rather than just electronic text. Receipt of timely and accurate information will enhance FDA's efforts to help ensure the integrity of the drug supply and protect public health.

Technical specifications for creation of the electronic files are provided in the following technical documents, which can be found on the FDA Data Standards Council website, *http://www.fda.gov/oc/datacouncil/spl.html*:

- *Structured Product Labeling Implementation Guide for FDA Drug Establishment Registration and Drug Listing*
- *Step-by-Step Instructions for Creating Structured Product Labeling (SPL) Files for Drug Establishment Registration and Drug Listing*
- *Structured Product Labeling Validation Procedures for Drug Establishment Registration and Drug Listing*

[10] These forms can be referenced at *http://www.fda.gov/opacom/morechoices/fdaforms/default.html*.

[11] When we are ready to receive a particular submission type in electronic format only, we generally identify the specific type of document that FDA can process, review, and archive. This information can be found in the public docket 92S-0251 at *regulations.gov*. See 21 CFR 11.2(b)(2); see also *Guidance for Industry: Part 11, Electronic Records; Electronic Signatures -- Scope and Application* (August 2003).

See also Section IV of this document for discussion of these specifications and other information on creating the drug establishment registration and drug listing file for electronic submission.

SPL format is already used for submission of content of labeling in electronic format as required in New Drug Applications (NDAs), Abbreviated New Drug Applications (ANDAs), Biological License Applications (BLAs), and annual reports on approved drugs.[12] See *Providing Regulatory Submissions in Electronic Format – Content of Labeling* (April 2005).[13] Because the content of labeling required under those provisions can be duplicative in content and format (SPL) of the labeling required to be submitted electronically as part of listing information, FDA encourages applicants to submit this labeling material, and updates, primarily through the drug establishment registration and drug listing system. Rather than make duplicate submissions, applicants are then encouraged to reference the SPL labeling file submitted through the electronic drug registration and listing system in making labeling updates to applications under the content of labeling requirements. FDA intends to issue guidance that will address this issue in further detail.

Beginning June 1, 2009, FDA intends to use the electronic drug establishment registration and listing system as the source of SPL to provide postapproval content of labeling for public access on the Web, making that system the key repository of this information.

III. DRUG ESTABLISHMENT REGISTRATION AND DRUG LISTING INFORMATION FOR ELECTRONIC SUBMISSION

The following information should be submitted to FDA in the SPL file format described in the technical documents and the defined code sets and codes as described in section IV of this document.

A. Drug Establishment Registration

1. Who must register, when, and how?

The owner or operator of an establishment entering into the manufacture, preparation, propagation, compounding, or processing (which includes, among other things, repackaging and relabeling) of a drug or drugs[14] and not exempt under section 510(g) of the Act or subpart B of 21 CFR part 207, must register the establishment with FDA within 5 days after beginning the operation (21 CFR 207.21(a) and 21 CFR 207.3(a)(8)). Alternatively, if the establishment has not previously entered into such an operation, the owner or operator must register within 5 days after submitting (among other things) a drug application, biological license application, or

[12] For regulations requiring submission of content of labeling in electronic format that FDA can process, review, and archive, see 21 CFR 314.50(l) (NDAs), 21 CFR 314.94(d) (ANDAs), 21 CFR 601.14(b) (BLAs), and 21 CFR 314.81(b) (annual reports to marketing applications).

[13] *http://www.fda.gov/cder/guidance/6719fnl.htm*

[14] Means both human, including biological drug products, and animal drugs.

medicated feed mill license application. (21 CFR 207.21(a)). Owners or operators must renew their registration information annually (Section 510(b)(1) of the Act; 21 CFR 207.21(a)).

Establishments within any foreign country that engage in the manufacture, preparation, propagation, compounding, or processing (which includes, among other things, repackaging and relabeling) of a drug that is imported or offered for import into the United States (and that are not exempt) must upon first engaging in such activity immediately register and register annually thereafter (Section 510(i) of the Act; 21 CFR 207.40).
Amendments to drug establishment registration must be submitted in accordance with 21 CFR 207.26.

Section 510(p) of the Act, as amended by FDAAA, now requires drug establishment registrations to be submitted electronically unless a waiver is granted. Therefore, registration information should now be submitted electronically using SPL files with coded data fields.[15]

Failure to register in accordance with section 510 of the Act is a prohibited act under section 301(p) of the Act. Also, under section 502(o) of the Act, a drug is misbranded if it is manufactured in an establishment in any State not duly registered under section 510 of the Act.

2. What information is submitted for drug establishment registration?

Section 510 of the Act and 21 CFR Part 207 set forth registration information required to be submitted by domestic and foreign drug establishments. (See sections 510(b), (c), (d), and (i) of the Act and 21 CFR 207.25(a), 21 CFR 207.26, and 21 CFR 207.40). Under these provisions, all registrants must provide the name and full address of each establishment, all trade names used by the establishment, the kind of ownership or operation (e.g., individually owned, partnership, or corporation), and the name of the owner or operator (including in the case of a partnership the name of each partner, and in the case of a corporation, the name and title of each corporate officer and director and the State of incorporation).

In addition to the information required for all registered establishments, certain additional information must be provided to register a foreign establishment. For example, a foreign registrant must submit:

- the name, address, and phone number of the foreign registrant's United States agent (Section 510(i)(1)(A) of the Act and 21 CFR 207.40)c));

- the name of each importer that is known to the establishment (Section 510(i)(1)(A) of the Act). (This means each U.S. company or individual in the United States that is an owner, consignee, or recipient of the foreign establishment's drug that is imported into the United States. An importer does not include the consumer or patient who ultimately

[15] As explained in section IV.C., of this document, once the SPL file is created it can be submitted (uploaded) by following the instructions for the FDA Electronic Submissions Gateway (ESG). There may be some delay in obtaining an ESG account; review section IV.C. for further information.

purchases, receives, or is administered the drug, unless the foreign establishment ships the drug directly to the consumer or patient.); and

- the name of each person who imports or offers for import such drug (Section 510(i)(1)(A) of the Act). (This means the name of each agent, broker, or other entity, other than a carrier, that the foreign drug establishment uses to facilitate the import of their drug into the United States).

To facilitate correspondence between registrants and FDA, foreign registrants should submit the email address for the U.S. agent, and the telephone number(s) and email address for the importer and person who imports or offers for import described in section III.A.2 of this document.

Historically, registrants have also included additional drug establishment registration information when making submissions, using Form FDA 2656.[16] Likewise, for electronic submission, registrants should submit the following additional information in their SPL file:

- Official contact's name, mailing address, telephone number(s), and email address; and
- The type of operation(s) performed at each establishment.

Under section 510(e) of the Act, FDA may assign a registration number to any person or registered establishment. FDA intends to use the Data Universal Numbering System (D-U-N-S®) as the registration number for the electronic system. Therefore, to facilitate and expedite processing of the SPL file, the registrant should submit their D-U-N-S® Number with the registration information. If the business entity does not submit a D-U-N-S® Number with its submission, FDA intends to make arrangements for obtaining a D-U-N-S® Number for that entity. An explanation of the D-U-N-S® Number and how to obtain one is described in section IV.B of this document.

B. Drug Listing

1. Who must list, when, and how?

Registrants not exempt under 21 CFR 207.10 must submit the initial listing information for all drugs[17] in commercial distribution at the time of their initial registration of their establishment(s) (21 CFR 207.21(a)).

Failure to provide any listing information required by section 510(j) of the Act is a prohibited act under section 301(p). Also, under section 502(o) of the Act, a drug is misbranded if it was not included in a list required by section 510(j) of the Act.

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[16] See 21 CFR 207.22(a) and 21 CFR 207.25(a). As noted, with the amendment of section 510(p) of the Act in 2007, registration information is required to be submitted electronically. Therefore, submission of such information on a particular paper form is no longer acceptable (absent grant of a waiver), and information should instead be submitted in accordance with this guidance document. FDA intends to amend the regulations to conform to the changes in the underlying statutory provision.

[17] Registration and listing requirements for drugs should also be met for combination products that include a drug as a constituent part, and for drugs intended as a constituent part of a combination product, regardless of which FDA center has the lead for review of the combination product (See 21 U.S.C. 503(g); 21 CFR part 3).

Although FDA does not accept drug establishment registration information from private label distributors (PLDs),[18] PLDs may request their own NDC Labeler Code and elect to submit drug listing information to FDA. (21 CFR 207.20(b)). By submitting drug listing information, the PLD assumes full responsibility for compliance with the listing requirements. (21 CFR 207.20(b)) In such instances, at the time of submitting or updating drug listing information, private label distributors must certify to the registered establishment(s) that manufactured, prepared, propagated, compounded or processed (which includes, among other things, repackaging and relabeling) the listed drug(s) that the drug listing submission was made (21 CFR 207.20(b)). The certification to the registered establishment by the private label distributor may be satisfied using paper format. If a drug product is listed by the PLD, it should not also be listed by the owner(s) of the registered establishment(s) that manufactured, prepared, propagated, compounded or processed (which includes, among other things, repackaging and relabeling) the listed drug(s).

Registrants (and, if applicable, private label distributors) must update their drug listing information, and include drugs that have been introduced for commercial distribution and have not previously been listed (Section 510(j)(2) of the Act; 21 CFR 207.21(b); 21 CFR 20720(b)). Any updates must be submitted every June and December (Section 510(j)(2) of the Act; 21 CFR 207.21(b)). However, registrants (and, if applicable, private label distributors) are encouraged to submit updates through the registration and listing system more frequently as changes occur, including labeling updates required to be submitted under listing requirements (21 CFR 207.21(b); 21 CFR 207.22(b); 21 CFR 207.25; 21 CFR 207.30), or labeling submission needed to fulfill obligations for electronic submission of content of labeling in connection with approval applications. (See section II of this document and footnote 12.) As previously discussed in section II of this document, because the drug listing system is a key repository for labeling, it is particularly important to keep this information up to date.

Section 510(p) of the Act, as amended by FDAAA, now requires drug listing, including updates, to be submitted electronically unless a waiver is granted. Therefore, listing information should now be submitted electronically using SPL files with coded data fields.

The electronic drug establishment registration and drug listing system will permit FDA to electronically populate the Agency's listing databases and the NDC Directory and will, therefore, improve the inclusiveness and accuracy of these databases.

2. What information is submitted for drug listing?

Section 510 of the Act and 21 CFR Part 207 set forth the drug listing information required to be submitted by domestic and foreign drug establishments. (Section 510(j) of the Act; 21 CFR 207.25(b) and (c); 21 CFR 207.30; 21 CFR 207.31; 21 CFR 207.40). For representative

[18] "Private label distributor" or "PLD" means an owner or operator of an establishment not otherwise required to register under section 510 of the Act, but who distributes under its own label or trade name a drug manufactured or processed by a registered establishment. (See 21 CFR 207.20(b))

samples of advertising and labeling required under 21 CFR 207.25(b)(4) and (b)(5), only one need be submitted of each sample type, as described in 21 CFR 207.3(a)(9) and (a)(10).

Historically, registrants have also submitted additional drug listing information on Form FDA 2657 and Form FDA 2658.[19] Likewise, for electronic submission, registrants should submit the following additional information in their SPL file:

- Name of establishment(s) manufacturing or processing the listed drug and the type of operation(s) performed;
- DEA schedule;
- Route(s) of administration;
- Inactive ingredients;
- Marketing information (e.g., category, start/stop date)[20];
- Information related to the application (e.g., type and year of approval) or OTC monograph citation number; and
- Package size and type.

In addition to information that was previously submitted on Forms FDA 2657 and FDA 2658, the registrant should also submit:

- NDC Product Code for a Source Drug Repacked or Relabeled

Repackers and relabelers should submit the NDC Product Code for the source drug that is repacked or relabeled, in order to reference manufacturing establishment information submitted in the listing entry for the source drug.

- Unique Ingredient Identifiers (UNII) and other code sets

An explanation of UNII codes and other code sets and where they may be found is described in section IV.B of this document.

- Confidentiality Flag

Registrants (and, if applicable, private label distributor) may identify an inactive ingredient or the registrant's business relationship with an establishment that they view as confidential when submitting registration and listing information. Pursuant to a Freedom of Information Act request or on our own initiative, FDA will ultimately make determinations as to whether drug establishment registration and drug listing information can be disclosed to the public pursuant to

[19] See 21 CFR 207.22 and 21 CFR 207.25(b). As noted, with the amendment of section 510(p) of the Act in 2007, listing information is required to be submitted electronically. Therefore, submission of such information on particular paper forms is no longer acceptable (absent grant of a waiver), and information should instead be submitted in accordance with this guidance document. FDA intends to amend the regulations to conform to the changes in the underlying statutory provision.

[20] The expiration date of the last lot released to the marketplace is considered a stop-date.

the Trade Secrets Act, the Freedom of Information Act, and other applicable law (e.g., section 510(f) of the Act and 21 CFR 207.37).[21]

- Distinctive Characteristics of Certain Listed Drugs

Registrants (and, if applicable, private label distributors) should provide the following characteristics for the listed drug, when applicable. Registrants (or private label distributors) have previously provided these characteristics voluntarily as helpful information for the safe and effective use of their products.

  - Flavor

When applicable, the registrant (and, if applicable, private label distributor) should provide the flavor as a unique distinguishing characteristic of the listed drug. (Registrants have previously provided this information on Form FDA 2657 as an ingredient.)

  - Color

For liquid dosage forms, the registrant (and, if applicable, private label distributor) should provide the color as a unique distinguishing characteristic. This may be useful to assist in judging whether a change in color may indicate contamination or to avoid confusion of the intended color of a solution with contamination.

  - Image

For solid oral dosage forms, the registrant (and, if applicable, private label distributor) may submit an image of the actual dosage form. This information is helpful in identifying the drug, for example in order to help determine that the correct drug has been dispensed. The registrant can obtain instructions on obtaining the image and the proper format in the SPL file by following the instructions for technical assistance in section IV.D of this document.

IV. CREATING THE DRUG ESTABLISHMENT REGISTRATION AND DRUG LISTING FILE FOR ELECTRONIC SUBMISSION

A. Structured Product Labeling

SPL is the standard that FDA intends to use for the exchange of drug establishment registration and drug listing information and is based on the Health Level Seven (HL7) version 3 Reference Information Model (RIM) and the Clinical Document Architecture (CDA).

FDA uses SPL for electronic submissions of drug establishment registration and drug listing information. The technical details on using SPL for registration and listing are available in the

[21] Other elements of listing information, including the marketing date and application ,information described above, will help FDA to determine the confidentiality of listing information, including labeling, submitted for drugs still under premarket review.

document *Structured Product Labeling Implementation Guide for FDA Drug Establishment Registration and Drug Listing* (SPL Implementation Guide).

FDA has been accepting SPL files for certain product information since 2004, and vendors have provided solutions for creating SPL files ranging from basic software tools to comprehensive information management systems. Additionally, FDA has collaborated with GlobalSubmit on software to create SPL files based on XForms technology. Information on using the XForms is available in the document *Step-by-Step Instructions for Creating Structured Product Labeling (SPL) Files for Drug Establishment Registration and Drug Listing*.

These documents are on the FDA Data Standards Council website, *http://www.fda.gov/oc/datacouncil/spl.html*.

B. Code Sets and Codes

To facilitate FDA's ability to process, review, and archive electronic submissions, code sets and codes are used as a language that is recognized by a computer system. FDA has been working with a number of organizations to develop and maintain such code sets and codes used for submitting drug establishment registration and drug listing information electronically. Many code sets and codes are already available at the Data Standards Council website (*http://www.fda.gov/oc/datacouncil/spl.html*), and FDA is continuously updating these codes sets and adding codes. Information on the organizations that maintain the code sets for submitting drug establishment registration and drug listing information electronically and how to obtain the code sets and codes used for electronic drug registration and listing follows.

1. Unique Ingredient Identifiers (UNII)

UNII is the defined code FDA uses for ingredients/substances. FDA along with United States Pharmacopeia (USP) maintains the UNII using the FDA Substance Registration System. These names and identifiers are accessible through USP website at *http://www.usp.org* and publications, the Data Standards Council website (*http://www.fda.gov/oc/datacouncil/spl.html*) and the NCI Thesaurus website at *http://evs.nci.nih.gov*. Additional ingredient identifiers may be requested through FDA by sending a request to *spl@fda.hhs.gov*.

2. Data Universal Numbering System (D-U-N-S®) Number[22]

Dun & Bradstreet assigns and maintains a database of the D-U-N-S® Numbers, which serve as unique identifiers (codes) of business entities. Upon application, each business entity (e.g., registrant, establishment, importer, US agent) is assigned a distinct site-specific 9-digit D-U-N-S® Number. The site-specific D-U-N-S® Number for an entity is a useful resource for FDA in identifying and verifying certain business information for that entity, e.g., trade names used by the entity, addresses, additional ownership information, such as the name of each partner or the

[22] D-U-N-S® Numbers are proprietary to and controlled by Dun & Bradstreet (D&B). Where practicable, the customer will refer to the number as a "D-U-N-S® Number" and state that D-U-N-S is a registered trademark of D&B.

name of each corporate officer and director, and the State of incorporation. If the D-U-N-S® Number for a location has not been assigned, a business may obtain one for no cost directly from Dun & Bradstreet (*http://www.dnb.com*). If the business entity does not submit a D-U-N-S® Number with its submission, FDA intends to make arrangements for obtaining a D-U-N-S® Number for that entity.

3. Other code sets

FDA collaborates with the National Cancer Institute Enterprise Vocabulary Services (NCI EVS) to maintain code sets for dosage form, routes of administration, package types, DEA schedule, product color, product shape, flavors, business operations, marketing categories and equivalence codes. These code sets are located in the NCI Thesaurus and may be accessed through the NCI EVS website at *http://evs.nci.nih.gov* and the Data Standards Council website (see section II of this document). Additional code sets and codes for use in registration and listing may be requested though FDA by sending a request to *spl@fda.hhs.gov*.

The Regenstrief Institute[23] maintains a number of different code sets used in electronic drug establishment registration and drug listing including: document types, section headings, and units of measure. These code sets are located in the Logical Observation Identifiers Names and Codes (LOINC) and Unified Codes for Units of Measure (UCUM) systems. Both of these terminologies are available at *http://www.regenstrief.org* and at other locations. Additional code sets and codes may be requested through FDA by sending a request to *spl@fda.hhs.gov* following the instructions in section IV.D of this document.

C. Submission and FDA Validation of Electronic Drug Establishment Registration and Drug Listing Information

The SPL file should be created following the technical specifications in the SPL Implementation Guide and other information found in this document. Other resources for creating the SPL file, including a link to a user-friendly software tool (XForms), are also available.[24] Once the SPL file is created, it can then be submitted (uploaded) by following the instructions for the FDA Electronic Submissions Gateway (ESG), including digital certification.[25]

The process for establishing an ESG account may involve a delay before drug registration and listing information can be received electronically by FDA. FDA encourages owners and operators subject to registration and listing to establish their ESG accounts as soon as possible; establishing an ESG account 4-6 weeks in advance of the time when the owner or operator must register, list, or update a registration or listing will best ensure that electronic submissions are not delayed.

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[23] The Regenstrief Institute is an internationally recognized informatics and healthcare research organization.

[24] See *http://www.fda.gov/oc/datacouncil/spl.html* for additional resources, terminology, and data standards regarding the SPL files. See *http://www.fda.gov/oc/datacouncil/xforms.html* for information on the user-friendly software tool.

[25] See *http://www.fda.gov/esg/default.htm* for information on other resources and using the FDA ESG.

FDA recognizes that there may be a delay between the time an owner or operator requests an ESG account and the time the account is established and can upload submissions. Provided the owner or operator requests an ESG account before the due date of their first electronic submission, FDA intends to exercise enforcement discretion and does not intend to initiate action based on a first electronic submission that is late if the owner or operator also makes the required submission (e.g., registration, listing, or update) within 30 days following establishment of an ESG account.

FDA uses a computer system for processing the SPL files using controlled code sets and codes. The computer system automatically checks the SPL files for certain errors, mistakes and omissions prior to entering the information into FDA systems. FDA will work with companies to help correct identified problems in order to complete the registration and listing process. Information on the details used in checking SPL files for electronic drug establishment registration and drug listing are in the document *FDA's Structured Product Labeling Validation Procedures for Electronic Drug Establishment Registration and Drug Listing*.[26] This document is on the Data Standards Council website (see section II of this document).

D. Technical Assistance

For technical problems or assistance with creating SPL files, send an email to *spl@fda.hhs.gov*.

V. IMPLEMENTATION

Beginning June 1, 2009, FDA intends to no longer accept drug establishment registration and drug listing information in paper format unless a waiver is granted.

VI. WAIVER REQUEST

Under section 510(p) of the Act, registrations and listings (including the submission of updated information) must be submitted electronically unless FDA grants a waiver of such requirement because use of electronic means is not reasonable for the person requesting such waiver. FDA does not anticipate many instances in which electronic submission of registration and listing information will not be reasonable for the person requesting the waiver. However, if you are granted a waiver, you will be instructed as to how to submit the registration and listing information.

To apply for a waiver from the requirement to electronically submit drug establishment registration and drug listing information, provide a written request with a complete explanation of why use of electronic means is not reasonable for you. Submit the request to:

[26] This document is used by FDA and describes FDA's computer instructions for automating the validation of submitted SPL files containing registration and listing information.

SPL Coordinator
U.S. Food and Drug Administration (HF-18)
5600 Fishers Lane
Rockville, MD 20857-0001

Phone: 1-888-463-6332

VII. PAPERWORK REDUCTION ACT OF 1995

This guidance contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520),

The time required to complete this information collection is estimated to average 4.5 hours per response, including the time to review instructions, search existing data sources, gather the data needed, and complete and review the information collection. Send comments regarding this burden estimate or suggestions for reducing this burden to *spl@fda.hhs.gov*.

This guidance also refers to previously approved collections of information found in FDA regulations. The collections of information in Part 207 have been approved under OMB Control No. 0910-0045.

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. The OMB control number for this information collection is 0910-0045 (expires 3/31/2012).