REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION

0910-0045

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

Requirements for drug establishment registration and drug listing are set forth in section 510 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360), section 351 of the Public Health Service Act, and part 207 (21 CFR part 207). 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.

Under section 510 of the FD&C Act, FDA is authorized to establish a system for registration of producers of drugs and for listing of drugs in commercial distribution. To implement section 510 of the FD&C Act, FDA issued part 207. Under current § 207.20, manufacturers, repackers, and relabelers that engage in the manufacture, preparation, propagation, compounding, or processing of human or veterinary drugs and biological products, including bulk drug substances and bulk drug substances for prescription compounding, and drug premixes as well as finished dosage forms, whether prescription or over-the-counter, are

required to register their establishment. In addition, manufacturers, repackers, and relabelers are required to submit a listing of every drug or biological product in commercial distribution. Owners or operators of establishments that distribute under their own label or trade name a drug product manufactured by a registered establishment are not required either to register or list. However, distributors may elect to submit drug listing information in lieu of the registered establishment that manufactures the drug product. Foreign drug establishments must also comply with the establishment registration and product listing requirements if they import or offer for import their products into the United States.

Under current § 207.21, establishments, both domestic and foreign, must register with FDA within 5 days after beginning the manufacture of drugs or biologicals, or within 5 days after the submission of a drug application or biological license application (BLA). In addition, establishments must register annually. Changes in individual ownership, corporate or partnership structure, location, or drug-handling activity must be submitted as amendments to registration under current § 207.26 within 5 days of such changes. Under § 207.20(b), private label distributors may request their own labeler code and elect to submit drug listing information to FDA. In such instances, at the time of submitting or updating drug listing information, private label distributors must certify to the registered establishment that manufactured, prepared, propagated, compounded or processed (which includes, among other things, repackaging and relabeling) the listed drug that the drug listing submission was made. Establishments must, within 5 days of beginning the manufacture of drugs or biologicals, submit to FDA a listing for every drug or biological product in commercial distribution at that time. Private label distributors may elect to submit to FDA a listing of every drug product they place

in commercial distribution. Registered establishments must submit to FDA drug product listing for those private label distributors who do not elect to submit listing information.

Under § 207.25, product listing information submitted to FDA by domestic and foreign manufacturers must, depending on the type of product being listed, include any new drug application (NDA) number or biological establishment license number, copies of current labeling and a sampling of advertisements, a quantitative listing of the active ingredient for each drug or biological product not subject to an approved application or license, the NDC number, and any drug imprinting information.

In addition to the product listing information required, FDA may also require, under § 207.31, a copy of all advertisements and a quantitative listing of all ingredients for each listed drug or biological product not subject to an approved application or license; the basis for a determination, by the establishment, that a listed drug or biological product is not subject to marketing or licensing approval requirements; and a list of certain drugs or biological products containing a particular ingredient. FDA may also request, but not require, the submission of a qualitative listing of the inactive ingredients for all listed drugs or biological products, and a quantitative listing of the active ingredients for all listed drugs or biological products subject to an approved application or license.

Under § 207.30, establishments must update their product listing information every June and December or, at the discretion of the establishment, when any change occurs. These updates must include the following information: (1) A listing of all drug or biological products introduced for commercial distribution that have not been included in any previously submitted list; (2) all drug or biological products formerly listed for which commercial distribution has

been discontinued; (3) all drug or biological products for which a notice of discontinuance was submitted and for which commercial distribution has been resumed; and (4) any material change in any information previously submitted. No update is required if no changes have occurred since the previously submitted list.

Historically, drug establishment registration and drug listing information have been submitted in paper form using 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) (collectively referred to as FDA Forms). Changes in the FD&C Act resulting from enactment of the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110-85) (FDAAA) require that drug establishment registration and drug listing information be submitted electronically unless a waiver is granted. Before the enactment of FDAAA, section 510(p) of the FD&C Act expressly provided for electronic submission of drug establishment registration information upon a finding that electronic receipt was feasible, and section 510(j) of the FD&C Act provided that drug listing information be submitted in the form and manner prescribed by FDA. Section 224 of FDAAA, which amends section 510(p) of the FD&C Act, now expressly, requires electronic drug listing in addition to drug establishment registration. In certain cases, if it is unreasonable to expect a person to submit registration and listing information electronically, FDA may grant a waiver from the electronic format requirement.

In the Federal Register of June 1, 2009 (74 FR 26248), FDA announced the availability of a guidance for industry entitled “Providing Regulatory Submissions in Electronic Format—Drug Establishment Registration and Drug Listing” (the 2009 guidance). The document

provides guidance to industry on the statutory requirement to submit electronically drug establishment registration and drug listing information. The guidance describes the types of information to include for purposes of drug establishment registration and drug listing and how to prepare and submit the information in an electronic format (Structured Product Labeling (SPL) files) that FDA can process, review, and archive. In addition to the information that previously was collected on the FDA Forms, the guidance addresses electronic submission of other required information as follows:

- For registered foreign drug establishments, the name, address, and telephone number of its U.S. agent (§ 207.40(c));
- The name of each importer that is known to the establishment (the 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 purchases, receives, or is administered the drug, unless the foreign establishment ships the drug directly to the consumer or the patient) (section 510(i)(1)(A) of the FD&C Act); and
- The name of each person who imports or offers for import (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) (section 510(i)(1)(A) of the FD&C Act).

FDA also recommends the voluntary submission of the following additional information, when applicable:

- To facilitate correspondence between foreign establishments and FDA, 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 their drug;
- A site-specific Data Universal Numbering System (DUNS) number for each entity (e.g., the registrant, establishments, U.S. agent, importer);
- The NDC product code for the source drug that is repacked or relabeled;
- Distinctive characteristics of certain listed drugs, i.e., the flavor, the color, and image of the actual solid dosage form; and
- Registrants may indicate that they view as confidential the registrant's business relationship with an establishment, or an inactive ingredient.

In addition to this collection of information, there is an additional burden for the following activities:

- Preparing a standard operating procedure (SOP) for the electronic submission of drug establishment registration and drug listing information;
- Creating the SPL file, including accessing and reviewing the technical specifications and instructional documents provided by FDA (accessible at *http://www.fda.gov/oc/datacouncil/spl.html*);
- Reviewing and selecting appropriate terms and codes used to create the SPL file (accessible at *http://www.fda.gov/oc/datacouncil/spl.html*);
- Obtaining the digital certificate used with FDA's electronic submission gateway and uploading the SPL file for submission (accessible at *http://www.fda.gov/esg/default.htm*); and

- Requests for waivers from the electronic submission process as described in the draft guidance.

2. Purpose and Use of the Information Collection

As discussed under the above section, fundamental to FDA's mission to protect the public health is the collection of this information, which is used for important activities such as post-market 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.

3. Use of Improved Information Technology and Burden Reduction

In the Federal Register of June 1, 2009 (74 FR 26248), FDA announced the availability of a guidance for industry entitled "Providing Regulatory Submissions in Electronic Format--Drug Establishment Registration and Drug Listing." As discussed above, the document provides guidance to industry on the statutory requirement to submit electronically drug establishment registration and drug listing information. The guidance describes the types of information to include for purposes of drug establishment registration and drug listing and how to prepare and submit the information in an electronic format (Structured Product Labeling (SPL) files) that FDA can process, review, and archive.

In addition, in the Federal Register of August 29, 2006 (71 FR 51276), FDA proposed to revise part 207. The proposed revisions would reorganize, consolidate, clarify, and modify

current regulations concerning who must register establishments and list, and describes when and how to register and list and what information must be submitted for registration and listing. In addition, the proposal would make certain changes to the National Drug Code (NDC) system and would require the appropriate NDC number to appear on the labels for drugs subject to the listing requirements. The proposed regulations also require the electronic submission of all registration and most listing information. The August 29, 2006, proposed rule requested comments on the information collection for revised part 207. When the proposal is finalized, the information collection for revised part 207 will replace the information collection in this notice.

4. Efforts to Identify Duplication and Use of Similar Information

Although several systems do exist in FDA that have related data, they exist for different uses. This information is not already submitted to the agency, and thus, there is no duplicate reporting.

5. Impact on Small Businesses or Other Small Entities

Data collection for purposes of this regulation may include small businesses. FDA has established a Division of Small Manufacturers Assistance to provide workshops, onsite evaluations, and other technical assistance to small manufacturers. Each FDA Field Office has small business representatives which help small businesses fill out forms, discuss regulatory requirements, and provide clarification to firm registration and drug listing matters.

6. Consequences of Collecting the Information Less Frequently

Information on the registration of drug firms and the listing of drug products cannot be collected less frequently. FDA believes that in order to fulfill its statutorily mandated responsibility under Section 510 of the Act, the agency needs to keep its listing current with changes in the industry.

7. Special Circumstances Relating to the Guidelines in 5 CFR 1320.5

None of the collection requirements are inconsistent with 5 CFR 1320.5(d)(2).

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of March 23, 2015 (80 FR 15214). FDA received one comment.

The comment noted that under § 207.20(a), manufacturers, repackers, and relabelers are required to register their establishment and submit a listing of every drug or biological product in commercial distribution. Under § 207.20(b), owners or operators of establishments that distribute under their own label or trade name a drug product manufactured by a registered establishment are not required either to register or list but may elect to submit drug listing information in lieu of the registered establishment that manufactures the drug product. The comment said that although the burden of listing private label drugs rests on the manufacturer, the standard industry practice has been to submit two separate listings under different marketing categories. The comment said that these listings are submitted either by the private label distributor or by the manufacturer and "in order for the necessary information to be provided to FDA (all Offices and Centers) both listings are necessary." The comment also recommended that all drug listings should include the marketing category of the drug.

(FDA Response). Under section 510 of the FD&C Act and 21 CFR 207, contract manufacturers (registered establishments) are required to list their products with FDA under their own labeler code. To properly identify such a listing, contract manufacturers should list products manufactured for a private label distributor by using one of following marketing categories: (1) Approved Drug Product Manufactured Exclusively For Private Label Distributor; (2) OTC Monograph Drug Product Manufactured Exclusively For Private Label Distributor; (3) Unapproved Drug Product Manufactured Exclusively For Private Label Distributor. Contract manufacturers may also include the private label distributor's labeling with the listing submission.

Additionally, 21 CFR 207.20(b) requires that the private label distributor have its product listed under its own labeler code (using whatever marketing category is appropriate to the finished product (e.g., NDA, OTC Monograph, Unapproved Drug)). The private label distributor may elect to do this on its own. If the private label distributor elects not to do this, then the responsibility for submitting the additional listing falls on the registered establishment (the contract manufacturer).

9. Explanation of Any Payment or Gift to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under this provision.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of drug listing information is safeguarded by 21 CFR 207.37.

11. Justification for Sensitive Questions

This information collection does not contain questions pertaining to sex, behavior, attitude, religious beliefs, or any other matters that are commonly considered private or sensitive in nature.

12. Estimates of Annualized Burden Hours and Costs

In the Federal Register of June 1, 2009 (74 FR 26248), FDA announced the availability of a guidance for industry entitled "Providing Regulatory Submissions in Electronic Format—Drug Establishment Registration and Drug Listing" (the 2009 guidance). The document provides guidance to industry on the statutory requirement to submit electronically drug establishment registration and drug listing information. The guidance describes the types of information to include for purposes of drug establishment registration and drug listing and how to prepare and submit the information in an electronic format (Structured Product Labeling (SPL) files) that FDA can process, review, and archive. In addition to the information that previously was collected on the FDA Forms, the guidance addresses electronic submission of other required information as follows:

- For registered foreign drug establishments, the name, address, and telephone number of its U.S. agent (§ 207.40(c));
- The name of each importer that is known to the establishment (the 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 purchases, receives, or is administered the drug, unless the

foreign establishment ships the drug directly to the consumer or the patient) (section 510(i)(1)(A) of the FD&C Act); and

- The name of each person who imports or offers for import (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) (section 510(i)(1)(A) of the FD&C Act).

FDA also recommends the voluntary submission of the following additional information, when applicable:

- To facilitate correspondence between foreign establishments and FDA, 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 their drug;
- A site-specific Data Universal Numbering System (DUNS) number for each entity (e.g., the registrant, establishments, U.S. agent, importer);
- The NDC product code for the source drug that is repacked or relabeled;
- Distinctive characteristics of certain listed drugs, i.e., the flavor, the color, and image of the actual solid dosage form; and
- Registrants may indicate that they view as confidential the registrant's business relationship with an establishment, or an inactive ingredient.

In addition to this collection of information, there is an additional burden for the following activities:

- Preparing a standard operating procedure (SOP) for the electronic submission of drug establishment registration and drug listing information;

- Creating the SPL file, including accessing and reviewing the technical specifications and instructional documents provided by FDA (accessible at *http://www.fda.gov/oc/datacouncil/spl.html*);
- Reviewing and selecting appropriate terms and codes used to create the SPL file (accessible at *http://www.fda.gov/oc/datacouncil/spl.html*);
- Obtaining the digital certificate used with FDA's electronic submission gateway and uploading the SPL file for submission (accessible at *http://www.fda.gov/esg/default.htm*); and
- Requests for waivers from the electronic submission process as described in the draft guidance.

When FDA published the 2009 guidance on submitting establishment registration and drug listing information in electronic format, the Agency also amended its burden estimates for OMB control number 0910-0045 to include the additional burden for the collection of information that had not been submitted using the FDA Forms, and to create and upload the SPL file. The amended burden estimates included the one-time preparation of an SOP for creating and uploading the SPL file. Although most firms will already have prepared an SOP for the electronic submission of drug establishment registration and drug listing information, each year additional firms will need to create an SOP. As provided in table 2 of this document, FDA estimates that approximately 1,000 firms will have to expend a one-time burden to prepare, review, and approve an SOP, and the Agency estimates that it will take 40 hours per recordkeeper to create 1,000 new SOPs for a total of 40,000 hours.

In the tables below, the information collection requirements of the drug establishment registration and drug listing requirements have been grouped according to the information

collection areas of the requirements.

Table 1.--Estimated Annual Reporting Burden					
Activity	No. of Respondents	No. of Responses Per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
New registrations, including new labeler codes requests	1,400	2	2,800	4.5	12,600
Annual updates of registration information	10,000	1	10,000	4.5	45,000
New drug listings	1,567	7	11,000	4.5	49,500
New listings for private label distributor	146	10.06	1,469	4.5	6,611
June and December updates of all drug listing information	5,300	20	106,000	4.5	477,000
Waiver requests	1	1	1	1	1
Total					590,712

Table 2.-- Estimated Annual Recordkeeping Burden					
Activity Resulting From Section 510(p) of the FD&C Act as Amended by FDAAA	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
One-time preparation of SOP	1,000	1	1,000	40	40,000
SOP maintenance	3,295	1	3,295	1	3,295
Total					43,295

13. Estimates of Other Total Annual Cost Burden to Respondents and/or Recordkeepers/Capital Costs

Based on an industry hourly wage average cost of $85 per hour, the annual cost is as follows:

Total burden hours of 584,507 @ $85 per hour equals $49,683,095.

14. Annualized Cost to the Federal Government

FDA currently devotes approximately 13 FTEs to maintaining the registration and listing database for human and veterinary drugs and biologics. If each FTE equals approximately $250,000, the total cost to the government is approximately $3,250,000.

15. Explanation for Program Changes or Adjustments

The change in burden hours results from revised, more accurate, registration and listing data information, resulting from the conversion from a paper to an electronic registration and listing system.

16. Plans for Tabulation and Publication and Project Time Schedule

No comprehensive tabulation of the data is planned or anticipated.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

The FDA Forms have been replaced with electronic submission of this information collection.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.