REGISTRATION OF PRODUCERS OF DRUGS AND LISTING OF DRUGS IN COMMERCIAL DISTRIBUTION -- 0910-0045
SUPPORTING STATEMENT

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) and section 351 of the Public Health Service Act (the PHS 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 act, FDA issued part 207.[1] 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

1 This document addresses the information collection in current part 207. 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 generally 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 document.

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. 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 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 National Drug Code 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 (Public Law 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 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 by 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 e-mail address for the U.S. agent, and the telephone number(s) and e-mail address for the importer and person who imports or offers for import their drug;
- A site-specific DUNS number for each entity (e.g., the registrant, establishments, U.S. agent, importer);
- The National Drug Code 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 the collection of information, there is 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 (ESG) 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 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 a standard operating procedure (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.

2. Purpose and Use of the Information Collection

As discussed under section # 1 above, 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.

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 the Federal Register of October 24, 2011 (76 FR 65730), FDA published a 60-day notice requesting public comment on the proposed collection of information. FDA received one comment.

Comment:

The comment raised two issues and asked for several procedural clarifications. The first issue raised suggested that the burden to industry might be greater than the 4.5 hour average provided in the estimate. The next issue questioned the process by which the FDA issued a guidance to address the electronic submissions process without changing the regulation that still

describes a paper submission process, which would have allowed for public comment on that change. The comment then sought several procedural clarifications on (1) how to submit changes in ownership of an establishment, (2) how to select a business function, (3) how to ensure that an establishment is represented consistently between a vendor's registration and the client's drug establishment registration, (4) how to link an importer with a particular product, (5) how to list bulk tablets that will be imported for packaging, and (6) how to certify to the registered establishment that the private label distributor has listed the product.

Response:

The FDA acknowledges that the 2009 Guidance entitled "Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing" is different from the process described in the current 21 CFR 207. As was stated in the Federal Register notice and acknowledged by the commentor, the current regulation predates the electronic process and describes a paper based submission process. The FDA is in the process of rewriting 21 CFR 207, and published the draft version which was published for public comment in 2006. Afterward, the Food and Drug Administration Amendments Act of 2007 (FDAAA) mandated the electronic submission of drug establishment and drug product information. The 2009 guidance was created to address the mandate of FDAAA. The 2006 draft rule will be modified appropriately to address the FDAAA mandates as well.

With regards to the estimated burden, the FDA collaborated with members of industry and international health information data standards organizations to arrive at the current process and estimates for the burden of gathering, assembling, and submitting data. The estimates are considered to be averages that will vary up or down per individual respondent.

(1) Changes to the establishment name, registrant name, or other registration information can be made by submitting an updated registration submission via structured product labeling (SPL). Changes in corporate ownership or officers that do not affect names, addresses, or the Data Universal Numbering System (DUNS) number(s) for a registered establishment should be

made with Dun and Bradstreet. That data is then referenced as needed by the FDA using the DUNS number. Information about submitting SPL can be found at the link at the end of the FDA response. It should be noted that changes in ownership may also require the submission of updates to listing information, labeler code name and DUNS, and application data for NDAs, ANDAs, BLAs, NADAs, and ANADAs.

(2) For selecting a business operation, a current list of valid business functions and their associated codes can be found at the link at the end of this response. Please note that if more than one business function apply, a registrant should select all that apply and include them in the registration SPL.

(3) The FDA has implemented an automated validation of all drug product listing submissions to ensure that each establishment referenced in the product listing is registered under the same business operation. For example, a product listing SPL that references a particular facility as a packer of the product will be rejected if that establishment has not chosen Pack as a business operation in its registration. The FDA expect vendors and clients to communicate this information directly to each other and, if necessary, coordinate their submissions in order to avoid issues with this validation.

(4) The importer information is submitted via the registration of the foreign establishment. Any product listing referencing that foreign establishment should therefore provide the necessary link from importer to product. Information about submitting SPL can be found at the link at the end of the FDA response.

(5) A product listing for bulk tablets intended for further processing or packaging should be listed using the SPL product/document type of Bulk Ingredient and a marketing category of Drug for Further Processing. Information about submitting SPL can be found at the link at the end of the FDA response.

(6) For finished dosage forms, appearance in the NDC Directory is proof of submission of listing. Note that unfinished products and active pharmaceutical ingredient (API) listings will

not appear in the Directory.

Instructions and SPL resources may be found on the SPL Resources webpage at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

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 Hour Burden and Costs

The information collection requirements of the Drug Listing and Establishment Registration regulations have been grouped according to the information collection areas of the regulations.

FDA estimates the burden of this collection of information as follows:

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	39	14.72	574	4.5	2,583
Annual updates of registration information	3,256	2.99	9,735	4.5	43,808
New drug listings	1,567	6.57	10,295	4.5	46,328
New listings for private label distributor	146	10.06	1,469	4.5	6,611
June and December updates of all drug listing information	1,677	11.21	18,799	4.5	84,596
Waiver requests	1	1	1	1	1
Total					183,927

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 Recordkeepers

Based on an industry hourly wage average cost of $75 per hour, the annual cost is as follows:

Total burden hours of 227,222 @ $75 per hour equals $17,041,650.

14. Annualized Cost to the Federal Government

FDA currently devotes approximately 30 FTEs to maintaining the registration and listing database for human and veterinary drugs and biologics. If each FTE equals approximately $160,000, the total cost to the government is approximately $4,800,000.

15. Explanation for Program Changes or Adjustments

The change in burden hours results from revised, more accurate, registration and listing data information, and steps taken to convert from a paper to an electronic information collection 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 involved in this collection will display the OMB expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification statement identified in Item 19, A Certification for Paperwork Reduction Act Submission, of OMB Form 83-I.

PAPERWORK REDUCTION ACT SUBMISSION

Please read the instructions before completing this form. For additional forms or assistance in completing this form, contact your agency's Paperwork Clearance Officer. Send two copies of this form, the collection instrument to be reviewed, the supporting statement, and any additional documentation to: Office of Information and Regulatory Affairs, Office of Management and Budget, Docket Library, Room 10102, 725 17th Street NW, Washington, DC 20503.

1. Agency/Subagency originating request

FDA

2. OMB control number b. [ ] None

a. 0910 - 0045

3. Type of information collection (*check one*)

a. [ ] New Collection

b. [ ] Revision of a currently approved collection

c. [x] Extension of a currently approved collection

d. [ ] Reinstatement, without change, of a previously approved collection for which approval has expired

e. [ ] Reinstatement, with change, of a previously approved collection for which approval has expired

f. [ ] Existing collection in use without an OMB control number

For b-f, note Item A2 of Supporting Statement instructions

4. Type of review requested (*check one*)

a. [x] Regular submission

b. [ ] Emergency - Approval requested by at close of comment period

c. [ ] Delegated

5. Small entities

Will this information collection have a significant economic impact on a substantial number of small entities? [ ] Yes [x] No

6. Requested expiration date

a. [X] Three years from approval date b. [ ] Other Specify:____/____

7. Title Registration of Producers of Drugs and Listing of Drugs in Commercial Distribution

8. Agency form number(s) (*if applicable*)

9. Keywords human drugs registration listing

10. Abstract 21 CFR part 207 implements section 510 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360), under which FDA is authorized to establish a system for registration of producers of drugs and for listing of drugs in commercial distribution.

11. Affected public (*Mark primary with "P" and all others that apply with "x")*

a. ___ Individuals or households d. ___ Farms

b. _x_ Business or other for-profit e. ___ Federal Government

c. ___ Not-for-profit institutions f. ___ State, Local or Tribal Government

12. Obligation to respond (*check one*)

a. [ ] Voluntary- (guidance document)

b. [x] Required to obtain or retain benefits

c. [Mandatory

13. Annual recordkeeping and reporting burden

a. Number of respondents 3,300

b. Total annual responses 40,873

1. Percentage of these responses collected electronically 100%

c. Total annual hours requested 227,222

d. Current OMB inventory 102,260 ___

14. Annual reporting and recordkeeping cost burden *(in thousands of dollars)*

a. Total annualized capital/startup costs 0

b. Total annual costs (O&M) 0

c. Total annualized cost requested 0

d. Current OMB inventory 0

e. Difference 124,962 f. Explanation of difference 1. Program change 2. Adjustment updated & purged database in preparation for conversion to EDRLS	e. Difference 0 f. Explanation of difference 1. Program change 2. Adjustment
15. Purpose of information collection (*Mark primary with "P" and all others that apply with "X"*) a. __ Application for benefits e.__ Program planning or management b. __ Program evaluation f.__ Research c. __ General purpose statistics g. x Regulatory or compliance d. __ Audit	16. Frequency of recordkeeping or reporting *(check all that apply)* a. [ ] Recordkeeping b. [ ] Third party disclosure c. [x] Reporting 1. [x] On occasion 2. [ ] Weekly 3. [ ] Monthly 4. [ ] Quarterly 5. [ ] Semi-annually 6. [x] Annually 7. [ ] Biennially 8. [x] Other (describe) one-time
17. Statistical methods Does this information collection employ statistical methods [ ] Yes [x] No	18. Agency Contact (person who can best answer questions regarding the content of this submission) Name: _____ Phone: _____

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