Establishment Registration of Producers of Drugs and
Listing of Drugs in Commercial Distribution

OMB Control No. 0910-0045; RIN 0910-AA49

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 (42 U.S.C. 262). Section 224 of Food and Drug Administration Amendments Act (FDAAA) amended section 510(p) of the FD&C Act to require electronic drug establishment registration and drug listing. Before the enactment of FDAAA, the FD&C Act provided for electronic submission of drug establishment registration information upon a finding that electronic receipt was feasible, and section 510(j) provided that drug listing information was to be prepared in the form and manner prescribed by FDA.

Under a proposed rule issued August 29, 2006 (71 FR 51276), FDA began to implement electronic submission of drug establishment registration and drug listing information consistent with statutory requirements. In 2009, we issued guidance entitled, "*Guidance for Industry; Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing*" describing the information to include for drug establishment registration and drug listing and providing instruction on how to prepare and submit the information in an electronic format (Structured Product Labeling (SPL) files) that FDA can process, review, and archive.

In the Federal Register of August 31, 2016 (81 FR 60170), we finalized the 2006 proposed rule setting forth drug establishment registration and listing requirements at 21 CFR part 207. The final rule entitled, "*Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs That Are Regulated Under a Biologics License Application, and Animal Drugs,*" codifies the statutory requirement for electronic submissions, adopting most of the provisions found in the proposed rule and discussed in the guidance. Specifically, the final rule describes how and when owners or operators of establishments at which drugs are manufactured or processed must register their establishments with FDA and list the drugs they manufacture or process. In addition, the rule makes certain changes to the National Drug Code (NDC) system. The final rule is intended to improve management of drug establishment registration and drug listing requirements and make these processes more efficient and effective for industry and FDA. Specific provisions of the rule and associated information collection are discussed below and may be found in the final rule at *Table 1 – Substantive Changes from the Proposed Rule to the Final Rule* on p. 60172 (81 FR 60172).

Forms 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* are retained for use in cases when a waiver has been granted.

2. Purpose and Use of the Information Collection

The information collection is used in support of FDA's mission to protect the public health through post-marketing surveillance for serious adverse drug reactions, inspection of drug manufacturing and processing facilities, and monitoring of drug products imported into the United States. The information collection also implements the electronic prescribing provisions of the Medicare Prescription Drug, Improvement, and Modernization Act of 2013 (MMA) and the availability of current drug labeling information through DailyMed, a computerized repository of drug information maintained by the National Library of Medicine.

3. Use of Improved Information Technology and Burden Reduction

The information collection establishes mandatory electronic reporting, however waivers may be issued in individual cases. Registration of establishments takes place annually during the period beginning on October 1 and ending on December 31. We estimate all respondents will submit the information electronically, unless exempted.

4. Efforts to Identify Duplication and Use of Similar Information

We are unaware of duplicative information collection.

5. Impact on Small Businesses or Other Small Entities

As explained in the Final Regulatory Flexibility Analysis (FRIA), the rulemaking does not impose a significant burden on a substantial number of small entities, and FDA certifies that the final rule will not have a significant economic impact on a substantial number of small entities.

6. Consequences of Collecting the Information Less Frequently

Information collection schedule is consistent with statutory requirements.

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

There are no special circumstances related to the information collection.

8. Comments in Response to the Proposed Rule and Efforts to Consult Outside the Agency

In the Federal Register of August 29, 2006 (71 FR 51276) FDA published a proposed rule entitled, "*Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs that are Regulated Under a Biologics License Application, and Animal Drugs*," including a PRA analysis and invited public comment. While several comments were received, none addressed the four information collection topics solicited in the proposal. Substantive comments are addressed in the agency's final rule that published August 31, 2016 (81 FR 60170) at *Section III* and may be found under Docket No. FDA–2005–N–0464 (formerly Docket No. 2005N–0403). FDA finalized the rule in the Federal Register of August 31, 2016 (81 FR 60170) and again invited public comment. None were received regarding the information collection.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

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

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimates

The agency estimates the annual burden as follows:

TABLE 1. Estimated Annual Reporting Burden[1]

Activity; 21 CFR Citation	No. of Respondents	No. of Responses Per Respondent	Total Annual Responses	Hours Per Response	Total Hours
Initial establishment registration; §§207.17, 207.21, 207.25	1,480	2	2,960	1	2,960
Annual review and update of registration information (including expedited updates); § 207.29	10,000	1	10,000	.50	5,000
Initial listing (including NDC); 207.33, 207.41, 207.45, 207.49, 207.53, 207.54, 207.55	1,713	7.28	12,470	1.5	18,705

Activity; 21 CFR Citation	No. of Respondents	No. of Responses Per Respondent	Total Annual Responses	Hours Per Response	Total Hours
June and December review and update (or certification) of listing; 207.35, 207.57	5,300	20	106,000	.75	79,500
Waiver requests; 207.65	1	1	1	.50	1
Public disclosure exemption requests; 207.81(c)	100	1	100	1	100
TOTAL	18,514		131,371		106,266

[1] There are no capital or operating and maintenance costs associated with the information collection.

TABLE 2. Estimated Annual Recordkeeping Burden[1]

SOP for creating and uploading the SPL file	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Avg. 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

[1] There are no capital or operating and maintenance costs associated with the information collection.

A. Registration Under Part 207

Under § 207.17, manufacturers, repackers, relabelers, and drug product salvagers must register their establishments. This is consistent with current registration information collection, except that PET drug producers are not exempt from registration under the final rule, and the final rule states that FDA will accept registration information from a private label distributor if it is acting as an authorized agent for and submitting information that pertains to an establishment that manufactures, repacks, relabels, or salvages drugs.

Under § 207.21, domestic manufacturers, domestic repackers, domestic relabelers, and domestic drug product salvagers must complete initial registration of each establishment no later than 5 calendar days after beginning to manufacture, repack, relabel, or salvage a drug. In addition, foreign manufacturers, foreign repackers, foreign relabelers, and foreign drug product salvagers must register each establishment before the drug is imported or offered for import into the United States.

The information that must be provided to FDA for registration is described in § 207.25 and includes the following:

(a) Name of the owner or operator of each establishment; if a partnership, the name of each partner; if a corporation, the name of each corporate officer and director, and the place of incorporation;

(b) Each establishment's name, physical address, and telephone number(s);

(c) All name(s) of the establishment, including names under which the establishment conducts business or names by which the establishment is known;

(d) Registration number of each establishment, if previously assigned by FDA;

(e) A Unique Facility Identifier in accordance with the system specified under section 510 of the Federal Food, Drug, and Cosmetic Act;

(f) All types of operations performed at each establishment;

(g) Name, mailing address, telephone number, and email address of the official contact for the establishment, as provided in §207.69(a); and

(h) Additionally, with respect to foreign establishments subject to registration, the name, mailing address, telephone number, and email address must be provided for:\

(1) The United States agent, as provided in §207.69(b);
(2) Each importer in the United States of drugs manufactured, repacked, relabeled, or salvaged at the establishment that is known to the establishment; and
(3) Each person who imports or offers for import such drug to the United States.

Also, the final rule lengthens the current time period for reporting changes to registration information from 5 days (10 business days for a change in U.S. agent information) to 30 calendar days. The final rule revokes the current requirement to report a change in individual ownership and corporate or partnership structure and the current requirement to submit a signed statement for a change in a registered establishment's firm name. Finally, new registration information collected under the final rule includes the certification that no changes have occurred and reporting certain changes as expedited updates within 30 calendar days.

Based on the number of new establishments that currently register each year, we estimate that approximately 1,400 registrants will submit electronically approximately 2,800 new establishment registrations annually. Based on the number of registered establishments in our database, we estimate that approximately 10,000 registrants will provide approximately 10,000 annual reviews and updates of registration information (including expedited updates) or reviews and certifications that no changes have occurred. The estimates include the registration of establishments for both domestic and foreign manufacturers, repackers, relabelers, and drug product salvagers, and registration information submitted by anyone acting as an authorized agent for an establishment that manufactures, repacks, relabels, or salvages

drugs. The estimates include an additional 80 PET drug producers who are not exempt from registration under the final rule and approximately 30 manufacturers of plasma derivatives.

We estimate that it will take approximately 1 hour for registrants to submit initial registration information electronically for each new establishment. We also estimate that it will take approximately 30 minutes for each annual review and update of registration information (including any expedited updates) or each review and certification that no changes have occurred. The burden hour estimates above are based on our familiarity with the amount of time it takes registrants to input registration information electronically since June 2009. The estimates are an average of the time it would take to register a domestic or foreign establishment and an average of the time it would take to review registration information and update several registration items in the database or review registration information and only certify that no changes have occurred.

B. Listing Under Part 207

Under § 207.41, registrants must list drugs they manufacture, repack, relabel, or salvage for commercial distribution. This requirement includes drug product salvagers not previously included. Also, the final rule revises NDC-related listing submissions as follows:

- A registrant must list each drug it manufactures, repacks, or relabels using an NDC that includes the registrant's own labeler code, regardless of whether the drug is commercially distributed under the registrant's own label or trade name or under the label or trade name of a private label distributor.

- Each registrant must list each drug it manufactures, repacks or relabels for commercial distribution under the trade name or label of a private label distributor using an NDC that includes such private label distributor's labeler code.
- During listing, each manufacturer, repacker, or relabeler must propose for assignment by FDA an NDC that includes its own labeler code for each package size and type of drug that it manufactures, repacks, or relabels for commercial distribution.

- If a drug is distributed under the trade name or label of a private label distributor, the manufacturer, repacker, or relabeler must also propose for assignment by FDA an NDC that includes the labeler code of the private label distributor under whose trade name or label the drug is distributed, for each package size and type so distributed.

- A manufacturer, repacker, relabeler, or private label distributor may also reserve a proposed NDC for a drug, before the drug is listed, by submitting certain information.

Under § 207.45, registrants must list, no later than 3 days after the initial registration of each establishment, any drug being manufactured, repacked, relabeled, or salvaged for commercial distribution at that establishment.

Under the final rule, the information the registrants must submit to list a drug, including the information that must be submitted (by a registrant or a private label distributor) to receive a labeler code, is described in §§ 207.33, 207.49, 207.53, 207.54, 207.55, and 207.61. Under part 207, we assign a labeler code to each registrant and the registrant assigns the product code and the package code for each drug product's NDC.

The listing and NDC information collections required by the final rule adds the following elements:

(1) The name of each inactive ingredient in a listed drug (assertions of confidentiality associated with individual inactive ingredients are covered in the electronic registration and listing guidance);

(2) Additional information, such as email address, to identify a domestic registrant (identifying information for foreign registrants is part of the electronic registration and listing guidance information collection and in current § 207.40(c));

(3) The drug master file or veterinary master file number, if one exists, must be submitted by the manufacturer for an unfinished drug;

(4) Drug product salvagers (who do not repack or relabel) must submit the lot number and expiration date and NDC assigned to the drug immediately before the drug is received by the drug product salvager;

(5) All new labeling for a repacked or relabeled drug must be submitted, and not only the changed labeling;

(6) Package type and volume information corresponding to the package code segment of the NDC must be submitted;

(7) A drug's OTC monograph reference (if any) and the date on which the drug was or will be introduced into commercial distribution are both requested for voluntary submission; and

(8) The name and UFI of the establishment where the registrant who lists the drug manufactures it and the type of operation performed on the drug at that establishment, and, if an immediate source NDC is not provided, the name and UFI of every other establishment where manufacturing is performed for the drug and the type of operation performed at each such establishment must be provided.

Under § 207.57, registrants must update drug listing information submitted previously (either when the change is made or, at a minimum, each June and December). Registrants must also notify FDA if any listed drug has been discontinued from marketing or if any discontinued drug has been reintroduced and provide listing information for any drug not yet listed (at the time of annual establishment registration if not sooner).

Under § 207.35, registrants must notify us of a change in any of the drug characteristics (except certain identifying information) for an NDC in § 207.33, and assign a new product code and package code for that drug.

Burden Estimates

Based on the number of drugs listed annually since June 2009, we estimate that approximately 1,713 registrants will submit electronically approximately 12,469 new listings annually (including the information submitted to obtain a labeler code and to reserve an NDC for future use).

Based on the number of drugs in our listing database and the current number of changes to listing information submitted, we estimate that approximately 5,300 registrants will provide approximately 10,000 June and 10,000 December reviews and updates of listing information--a total of approximately 20,000 submissions annually (including the information submitted to revise an NDC).

The estimates for the number of drug listings include both domestic and foreign listings, listings submitted by registrants for products sold under their own names as well as products intended for private label distribution, and information submitted related to an NDC and to obtain a labeler code. The estimate for the number of drugs subject to the listing requirements includes PET drugs and approximately 30 plasma derivatives. The estimates for the number of June and December reviews and updates of listing information include the number of changes to drug characteristics pertaining to the drug product code to obtain a new NDC and the reports of the withdrawal of an approved drug from sale under § 314.81(b)(3)(iii).

Based on our familiarity with the time required to input listing information electronically since June 2009, we estimate that it will take registrants approximately 1 hour and 30 minutes to submit information electronically for each drug they list for the first time (for both foreign and domestic registrant listings). These estimates are an average of the time it will take manufacturers, repackers, relabelers, and drug product salvagers, with drug product salvagers taking considerably less time than manufacturers. The estimates include the time for submitting the content of labeling and other labeling in electronic format. (For drugs subject to an approved marketing application, the electronic submission of the content of labeling under § 314.50(l)(1)(i) is approved under OMB Control Number 0910-0001). We also estimate that it will take approximately 45 minutes for each June and December review and update. These estimates represent the average amount of time it would take to review and update listing information or to review and certify that no changes have occurred. The estimates include the time for submitting any labeling for each drug, changes to the drug's characteristics submitted for a new NDC, and reports of the withdrawal of an approved drug from sale under § 314.81(b)(3)(iii).

12b. Annualized Cost Burden Estimates

The FRIA uses an hourly wage of $66.50 from the Bureau of Labor Statistics corresponding to management occupations in pharmaceutical and medicine manufacturing. This base wage is multiplied by a factor of two to adjust for benefits and overhead. The result is an adjusted wage of $133. By multiplying $133 times the total hours in the tables above, FDA estimates an annual cost burden of $19,891,613.

13. Estimates of Other Total Annual Cost Burden to Respondents and Recordkeepers

There are no start-up, operating, or maintenance costs associated with this information collection.

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 (fully-burdened), the total cost to government is approximately $3,250,000.

15. Explanation for Program Changes or Adjustments

This information collection is being revised by rulemaking (see Q8 for public notice and comment discussion). Individual collection provisions are discussed previously under Q12 of this supporting statement and more fully in the agency's final rule (81 FR 60170). Data elements of the collection have been modified to add, remove, expand, reduce, and clarify specific requirements, however we believe these changes are marginal and thus we have increased our estimated number of annual responses by just **292**. At the same time, and as explained in our proposed rule of August 29, 2006 (71 FR 51276, at 51341), having now allowed respondents time to become experienced with the electronic system, we have reduced our estimate of the time necessary for the respective reporting elements themselves. Thus, there is a cumulative reduction in the annual hourly burden by **484,307**.

Individual ICs have been modified as reflected in the table below. Specifically, IC 1 (*Initial Registration*) has been modified to include an estimated 80 additional respondents that represent producers of PET drugs who were not previously required to register under the proposed rule. Although discussed in the final rule publication (81 FR at 60207), the additional 80 respondents were inadvertently omitted from the burden table but are included at Q12 of this supporting statement.

IC 3, "*Initial Listing*" consolidates two previously itemized ICs (*new listings* and *new listings for private label distributor*) but, as discussed above, reduces time per reporting activity. IC 4 reflects new burden associated with § 207.81(c) – *requests for exemptions from public disclosure of certain information*, but eliminates burden now consolidated at IC 3.

IC 5 (*updates*) reflects no new reporting burden but, again as discussed above, we have reduced the associated time burden. The remaining ICs are unchanged and are associated with waiver requests and recordkeeping responsibilities.

	Responses	Hours
IC 1	160	-9,640
IC 2	0	-40,000
IC 3	1,501	-30,656
IC 4	-1,369	-6,511
IC 5,	0	-397,500
IC 6, 7, 8	0	0
TOTAL	292	-484,307

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected under this rulemaking will not be tabulated or published.

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

Display of OMB Expiration date is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.