SUPPORTING STATEMENT
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 – Proposed Rule

A. Justification

1. Circumstances of Information Collection

The proposed rule would reorganize, consolidate, clarify, and modify current regulations on registering establishments and listing human and animal drugs under 21 CFR 207, blood and blood products under part 607, and HCT/Ps under part 1271. The proposal describes when and how to register and list and what information must be submitted for registration and listing. The proposal makes certain changes to the NDC system for drugs and would require the appropriate NDC number to appear on drug labels (for drugs subject to the drug listing requirements). The proposed regulations would require the electronic submission of all registration and most listing information instead of the current use of paper forms.

Registration Information Under Proposed Part 207

Under proposed § 207.17, manufacturers, repackers, relabelers, and drug product salvagers must register establishments. This is consistent with current registration requirements, except that currently private label distributors may submit information (similar to registration information) to obtain a labeler code from FDA. In

addition, the estimates include PET drug producers who would not be exempt from registration under the proposal.

Under proposed § 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 U.S. This is consistent with current registration requirements, except that the proposal would include additional foreign establishments as a result of the revocation of the exemption for drugs that enter a foreign trade zone and are re-exported from that foreign trade zone without having entered U.S. commerce, and for drugs imported under section 801(d)(3) of the act.

The information that must be provided to FDA for registration is described under proposed § 207.25. The information that would be required under proposed § 207.25 differs from the information currently required for registration. The following currently required information would not be required under the proposal: The kind of ownership or operation and the title of each corporate officer and director. New information required under the proposal would be the type of operations performed at each establishment, and

contact information about the official contact and the United States agent, each importer of the drug that is known to the establishment, and each person who imports or offers for import the drug to the United States.

Under proposed § 207.29, manufacturers, repackers, relabelers, and drug product salvagers must review annually their registration information. During the review, manufacturers, repackers, relabelers, and drug product salvagers must report all changes to their registration information or certify that no changes have occurred. In addition to the annual review and update, manufacturers, repackers, relabelers, and drug product salvagers must submit expedited reports of certain changes within 30 calendar days of the change. Currently, manufacturers, repackers, relabelers, and drug product salvagers must renew their registration information annually and submit certain amendments to registration within 5 days of a change. Proposed § 207.29 differs from the current requirement to submit amendments to registration in the following ways: The proposal would lengthen the current time period for reporting changes to registration information from 5 days (10 business days for a change in United States agent information) to 30 calendar days. The proposal would revoke 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. New requirements under the proposal would be to certify that no changes have occurred and to report as expedited updates certain changes within 30 calendar days, such as the close or sale of an establishment. Modified requirements would be to submit within 30 calendar days a change in the name or address of an establishment and a change in contact information for the official contact and United States agent.

Listing Information Under Proposed Part 207

Under proposed § 207.41, manufacturers, repackers, relabelers, and drug product salvagers must list drugs they manufacture, repack, relabel, or salvage for commercial distribution (this includes drugs they manufacture, repack, relabel, or salvage for a private label distributor). This proposed requirement is consistent with the current listing requirements, except that drug product salvagers are not currently required to list under part 207 and private label distributors may submit listing information directly to FDA.

Under proposed § 207.45, manufacturers, repackers, relabelers, and drug product salvagers must list, at the time of initial registration of an establishment, any drug being manufactured, repacked, relabeled, or salvaged for commercial distribution at that establishment. This is consistent with the current listing requirements, except that drug product salvagers are not currently required to list under part 207.

Under the proposal, the human-readable NDC number must appear on the drug's label (for drugs subject to the listing requirements). The information that must be provided electronically by manufacturers, repackers, and relabelers (including drug product salvagers who repack and relabel) to receive an NDC number is described under proposed § 207.33. Currently, the human-readable NDC number is not required to appear on the drug's label, but most prescription drugs and about one-third of the OTC drug products have the NDC number on the label. FDA currently assigns a labeler code to each manufacturer, repacker, relabeler, and private label distributor to be part of the NDC number, and the manufacturer, repacker, relabeler, and private label distributor assigns the remainder of the NDC number to each drug product. Under the proposal, for drugs listed after the effective date of the proposal, the NDC number for a drug must be obtained from us before (or at the time) that drug is listed. Some of the information currently required to list the drug would be submitted under the proposal to receive the NDC number. The assigned NDC number would be submitted as part of the listing information and would serve as a link to the information already submitted for the drug to obtain the NDC number.

The information that must be provided electronically by manufacturers, repackers, and relabelers to list a drug is described under proposed §§ 207.49, 207.53, 207.54, 207.55, and 207.61. As

mentioned previously, drug product salvagers are not currently required to list the drugs they salvage. The listing information and the NDC number information required under the proposal is consistent with the information currently submitted to FDA on Forms FDA 2657 or 2658, except for the following: (1) The proposal would require identification information about the name of each importer of the drug that is known to the establishment and each person who imports or offers for import a drug to the United States (importer information is currently required under the Bioterrorism Act); (2) the content of labeling would be submitted electronically (for approved human drugs, the information collection burden for this requirement is accounted for under current § 314.50(l)(1)(i), approved under OMB Control Number 0910-0001); (3) the quantity of the active pharmaceutical ingredient would be required for all drugs subject to the listing requirements (unless the approved application number is provided) (this requirement is substantially the same as the current requirement); (4) the name of the inactive ingredients for certain drugs would be required under the proposal (unless the approved application number is provided); (5) repackers and relabelers would be required to submit the NDC number assigned to the drug immediately before they received the drug; (6) additional information to identify the manufacturer, repacker, relabeler, and drug product salvager would be required (such as e-mail address, fax

number, and labeler code); (7) the submission of a representative sampling of labeling would include advertisements under § 202.1(l)(1); (8) certain listing information would not have to be submitted if the approved U.S. application number for the drug is provided; (9) the DMF number would be submitted by the manufacturer to obtain an NDC number for an active pharmaceutical ingredient; and (10) drug product salvagers (who do not repack or relabel) would submit the lot number and expiration data and NDC number assigned to the drug immediately before the drug is received by the drug product salvager.

Under proposed § 207.57, manufacturers, repackers, relabelers, and drug product salvagers must review each June and December all drug listing information that has been provided to us and must report all material changes or certify that no changes have occurred. Manufacturers, repackers, and relabelers must also notify FDA at this time if any listed drug has been discontinued from marketing or if any discontinued drug has resumed marketing and provide listing information for any drug not yet listed. Under the proposal, all manufacturers, repackers, relabelers, and drug product salvagers must review the listing information for each drug listed and report any material changes. Current regulations do not specify that the information for each listed drug needs to be reviewed, nor is a certification required if there are no changes. Only material changes to listing information must be reported, and fewer changes

are considered "material" under the current requirements. Under the proposal and consistent with section 510 of the act, manufacturers, repackers, relabelers, and drug product salvagers must also update their listing information for drug products that have not been previously listed at the time registration information for each establishment is updated.

Under proposed § 207.33(f), manufacturers, repackers, and relabelers must notify us of a change in any of the drug characteristics (except certain identifying information) for an NDC number in §§ 207.33, and we would assign a new NDC number for that drug.

Under proposed § 314.81(b)(3)(iii), applicants under part 314 must report electronically within 30 calendar days the withdrawal of an approved drug product from sale (the current requirement is to report within 15 days).

Registration and Listing Information Under Proposed Part 607

Under proposed § 607.22, manufacturers may electronically obtain, complete, and submit to FDA Form FDA 2830 (Blood Establishment Registration and Product Listing) or may request a copy of the form by e-mail. Currently, under § 607.22, manufacturers must register establishments and list blood products on Form FDA 2830. The proposal is consistent with the current requirement to register establishments and list products approved under OMB Control Number

0910-0052.

Under proposed § 607.25(b)(1), blood establishments are required to list blood products by the established and proprietary name. This proposal is consistent with the current listing requirement approved under OMB Control Number 0910-0052. Currently, blood establishments list bulk product substances as well as finished dosage forms under both part 607 and 207 to obtain an NDC number. The proposal would reduce reporting burden by requiring blood establishments to list only under part 607. To be consistent with part 207, the proposal would also delete the reference in Part 607 to Form FDA 2250 (National Drug Code Directory Input) because this form is no longer being used by CDER or CBER.

Under proposed § 607.40, foreign establishments must register each establishment before their blood product enters a foreign trade zone and are re-exported from that foreign trade zone without having entered U.S. commerce. This proposal is consistent with the current registration requirement in that establishments must register before their blood products are imported or offered for import into the United States. The proposal would also include additional foreign establishments as a result of the revocation of the exemption under section 801(d)(4) of the act for blood products that enter a foreign trade zone and are re-exported from that foreign trade zone without having entered U.S. commerce. The proposal would require additional

information for each foreign establishment. The proposal would also require the foreign establishment to report to FDA changes in the U.S. agent's name, address, telephone and fax numbers, and e-mail address within 30 calendar days of the change. The proposal would lengthen the time period from 10-business days to 30 calendar days for reporting changes in the U.S. agent to FDA.

Registration and Listing Information Under Proposed Part 1271

Under proposed § 1271.22, establishments must register, list products, and provide updates electronically. The current regulation requires registration, listing, and updates either electronically or in paper form using Form FDA 3356 and is approved under OMB Control Number 0910-0469.

Under proposed § 1271.25, establishments would submit the telephone and fax numbers, and e-mail address of the reporting official. Each foreign establishment would submit the name, the address, telephone and fax numbers, and e-mail address of each importer that is known to the establishment and the name of each person who imports or offers for import such HCT/P to the United States. Foreign establishments would also submit the name, the address, telephone and fax numbers, and e-mail address of their U.S. agent.

Under proposed § 1271.26, establishments must report a change to the U.S. agent's name, address, telephone and fax number, and e-mail

address. The proposal would also lengthen to 30 calendar days the current requirement of reporting the changes within 5 days.

User Account Information for Electronic System

Under proposed § 207.61, establishment registration and drug listing information must be submitted in electronic format. In addition, the content of labeling must be submitted in electronic format. Other labeling and advertisements may be provided in paper or electronic format. Electronic format submissions must be in a form that FDA can process, review, and archive. Prior to accepting registration and listing information from the online system, FDA may need to authenticate the source (that is, manufacturer, repacker, relabeler, or drug product salvager) providing the data. Under the proposal, FDA would authenticate entry into the electronic drug registration and listing system by establishing user accounts based on the current registration information. FDA would contact currently registered manufacturers, repackers, relabelers, or drug product salvagers and request that they provide electronic contact information to establish an administration account.

Waiver Request Information - Part 207

Under proposed § 207.65, manufacturers, repackers, relabelers, and drug product salvagers may request a waiver from the requirement in § 207.61 that information must be provided in electronic format. FDA expects very few waiver requests because only a computer,

Internet access, and an email address are needed to register and list.

Waiver Request Information - Part 607

Under proposed § 607.40(f)(1), foreign establishments may request a waiver from the requirement in § 607.40(e) that information must be provided to FDA in electronic format. FDA expects very few waiver requests because only a computer, Internet access, and an e-mail address are needed to register and list.

Waiver Request Information - Part 1271

Under proposed § 1271.23, manufacturers may request a waiver from the requirement in § 1271.22 that information must be provided to FDA in electronic format. FDA expects few waiver requests because only a computer, Internet access, and an e-mail address are needed to register and list.

Public Disclosure Exemption Requests

Under proposed § 207.81(c), manufacturers, repackers, relabelers, and drug product salvagers may request that certain information in proposed § 207.81(a) not be made available from their registration and listing information.

Revised Labeling Submitted With Annual Report

Under the proposal, the NDC number must appear on all drug labels for drugs subject to the listing requirements. Manufacturers, repackers, and relabelers for drug products that do not already have

an NDC number on the label would be required to include the NDC number assigned by FDA. Manufacturers, repackers, and relabelers for drug products that have an NDC number on the label as it is currently required would be required to examine their current NDC number to ensure that it complies with the NDC number requirements in proposed §§ 201.2, 207.33, and 207.37, and would have to obtain a new NDC number from us if necessary.

2. Purpose and Use of Information

FDA's database establishment registration and drug listing information is intended to provide complete and accurate registration and listing information to accomplish a number of statutory and regulatory objectives. For example:

- Identify the manufacturers, repackers, relabelers, and drug product salvagers of marketed drugs;[1]

- Identify the manufacturers, repackers, or relabelers of a specific drug or ingredient when that drug or ingredient is in short supply or is needed for a national emergency. This information helps facilitate prompt drug shipment to the place where it is needed. For

1 "Drug" or "drugs" refers to human drugs, including drugs that are regulated under a biologics license application, and animal drugs (including Type A medicated articles), unless otherwise specifically stated. "Drugs" is defined in proposed § 207.1 and discussed in section IV.A.5 of this document. Biological products subject to proposed part 207 are described in proposed § 207.9(c).

example, during a bioterrorism incident, FDA could use drug listing information to identify manufacturers, repackers, and relabelers of drugs that would be helpful in preventing or counteracting the deadly effects of biological weapons. With this information, FDA could facilitate prompt shipment of the drugs as needed;

- Facilitate the recall of drugs marketed by manufacturers, repackers, and relabelers;
- Identify and catalogue marketed drugs;
- Administer our postmarketing surveillance programs for drugs, including the drug surveillance sampling program that monitors the quality of the national drug supply;
- Identify drugs marketed in violation of the law;
- Schedule and plan inspections of registered establishments pursuant to section 704 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 374); and
- Determine which marketed drugs are identical, related, or similar to drugs reviewed for effectiveness under the Drug Efficacy Study Implementation (DESI) program.

Registration and listing information also helps with FDA's compliance with several other statutory provisions:

- Determine which entities are subject to establishment and product user fees under the prescription drug user fee program and the animal drug user fee program (21 U.S.C.379h and 379).

- Generate accurate estimates of the number of manufacturers, repackers, relabelers, and drug product salvagers and drugs that are affected by FDA rulemaking. These estimates help to assess the impact of regulations on the regulated industry, as required under the Regulatory Flexibility Act (5 U.S.C. 601-612), as amended by the Small Business Regulatory Enforcement Fairness Act (Public Law 104-121), the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 et seq.), the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520), Executive Order 12866 (September 30, 1993), and the Congressional Review Act (section 251 of Public Law 104-121).

3. Use of Improved Information Technology

Recent technological advances would allow FDA to enhance the usefulness of registration and listing information. Specifically, FDA is proposing that registration and listing information be submitted to the agency by using the electronic drug registration and listing system that FDA intends to develop. In addition to making the registration and listing process more efficient for industry, the electronic submission of registration and listing information would allow FDA to review and use such information more quickly and

effectively in carrying out all of the activities described in section 2 above. Electronic submission of this information would also allow FDA to fully support the implementation of the provisions of the Medicare Prescription Drug, Improvement, and Modernization Act (Public Law 108-173) (Medicare Modernization Act), specifically the electronic prescribing provisions. In addition, electronic submission of registration and listing information would further the purpose of several statutes:

- The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188) (Bioterrorism Act) amended section 510(i) of the act (21 U.S.C. 360(i)) to require that foreign establishments submit, among other things, registration information electronically.

- The Medical Device User Fee and Modernization Act of 2002 (Public Law 107-250) also amended section 510 of the act (at section 510(p)) to explicitly give the Secretary of Health and Human Services (the Secretary) discretion to require the electronic submission of registration information, upon a finding that electronic receipt of such registration information is feasible, unless the Secretary grants a request for a waiver.

- The Government Paperwork Elimination Act of 1998 (Public Law 105-277, Title XVII)(GPEA) requires Federal agencies to give persons

who are required to maintain, submit, or disclose information the option of doing so electronically when practicable as a substitute for paper, and to use electronic authentication (electronic signature) methods to verify the identity of the sender and the integrity of the electronic content.

Conversion to the electronic submission of registration and listing information will further the purpose of these laws and make the registration and listing processes more efficient and effective for industry and FDA.

4. Efforts to Identify Duplication

This information is not otherwise submitted to the agency, and thus, there is no duplicate reporting.

5. Involvement of Small Entities

As explained in section VI (Analysis of Economic Impacts) of the proposed rule, the proposed rule is unlikely to have a significant impact on a substantial number of small entities.

6. Consequences If Information Collected 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 registration and listing information current with changes in the industry.

7. Consistency with the Guidelines in 5 CFR 1320.5(d)(2)

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

8. Consultation Outside the Agency

The public will have the opportunity to comment on the proposed rule. All comments will be summarized and responded to in the final rule.

9. Remuneration of Respondents

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

10. Assurance of Confidentiality

Confidentiality of drug listing information is safeguarded by proposed § 207.81.

11. Questions of a Sensitive Nature

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

FDA currently reviews completed registration and listing forms and other submissions required under current parts 207, 607, and 1271. The information collection for current part 207 is approved by OMB until December 31, 2007, under OMB Control Number 0910-0045. The information collection for current part 607 and Form FDA 2830 is approved by OMB until March 31, 2009, under OMB Control Number 0910-0052. The information collection for current part 1271 and Form FDA 3356 is approved by OMB until July 31, 2007, under OMB Control Number 0910-0469.

FDA has estimated, in Tables 1, 2, and 3 of this document, the burden to comply with all of the information collection requirements for proposed part 207, 607, and 1271. These estimates are based on FDA's experience in reviewing registration and listing submissions and on the number of submissions currently received, the number of respondents submitting this information, and the number of registered establishments and listed drugs, blood products, and HCT/Ps currently in FDA's database. The estimates discussed below are for each section of proposed parts 207, 607, and 1271 that contain a reporting burden under the PRA.

Registration Information Under Part 207 - Burden Estimates

Based on the number of new establishments that currently register each year by submitting Form FDA 2656, we estimate that approximately 987 manufacturers, repackers, relabelers, and drug product salvagers will provide electronically approximately 1,128 new establishment registrations annually. Based on the number of registered establishments in the FDA database, we estimate that approximately 8,343 manufacturers, repackers, relabelers, and drug product salvagers will provide approximately 12,137 annual reviews and updates of registration information or reviews and certifications that no changes have occurred. Based on the number of changes to registration information that have been submitted annually on Form FDA 2656e, we estimate that approximately 775 manufacturers, repackers, relabelers, and drug product salvagers will provide approximately 1,921 expedited updates.

The estimates include the registration of establishments for both domestic and foreign manufacturers, repackers, relabelers, and drug product salvagers. The estimates for the number of manufacturers, repackers, relabelers, and drug product salvagers excludes the number of private label distributors currently in the database that submit information to receive a labeler code. The estimates include an additional 80 PET drug producers who would not be exempt from registration under the proposal, and approximately 30

manufacturers of plasma derivatives. In addition, the estimates include five additional foreign establishments that would be required to register as a result of the revocation of the exemption for drugs that enter a foreign trade zone and are re-exported from that foreign trade zone without having entered U.S. commerce, and for drugs imported under section 801(d)(3) of the act.

We estimate that it will take approximately 60 minutes to provide electronically the initial registration information for each new establishment. This estimate is only until manufacturers, repackers, relabelers, and drug product salvagers become familiar with using the electronic drug registration and listing system. We intend to lower this burden estimate to approximately 30 minutes when we submit to OMB the request to renew approval of this information collection.

We also estimate that it will take approximately 30 minutes for each annual review and update of registration information or each review and certification that no changes have occurred. This estimate is only until manufacturers, repackers, relabelers, and drug product salvagers become familiar with using the electronic drug registration and listing system. We intend to lower this burden estimate to approximately 15 minutes when we submit to OMB the request to renew approval of this information collection.

We also estimate that it will take approximately 15 minutes to

provide each expedited update. This estimate is only until manufacturers, repackers, relabelers, and drug product salvagers become familiar with using the electronic drug registration and listing system. We intend to lower this burden estimate to approximately 5 minutes when we submit to OMB the request to renew approval of this information collection.

The burden hour estimates above are based on our familiarity with the content of current registration forms and submissions and the times required by industry volunteers to input registration information during our electronic drug registration and listing system pilot project (discussed in section IV.E.3 of this document). 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. We note that these estimates for the electronic submission of this information would be a reduction in the currently approved estimate of 2.50 hours (OMB Control Number 0910-0045) for preparing and mailing to FDA Form FDA 2656.

We intend to migrate into our new database current registration information that had been submitted using paper forms. As a result, current manufacturers, repackers, relabelers, and drug product

salvagers would require additional time to review in the new database all current registration information and make any necessary revisions. We assume that this one-time initial review will be the first annual review and update using the electronic system, and we estimate it will take an average of 30 minutes for each review and update.

Listing Information Under Part 207 - Burden Estimates

Based on the current receipts of Forms FDA 2657 and 2658 for new listings, we estimate that approximately 1,812 manufacturers, repackers, relabelers, and drug product salvagers will provide electronically approximately 13,821 new listings annually.

Based on the number of drugs in our listing database and the current receipts of Forms FDA 2657 and 2658 for changes to listing information (and, until recently, the number of receipts of compliance verification reports), we estimate that approximately 2,278 manufacturers, repackers, relabelers, and drug product salvagers will provide approximately 22,568 June and 22,568 December reviews and updates of listing information (a total of 45,136 submissions annually), and that approximately 5,594 manufacturers, repackers, relabelers, and drug product salvagers will provide approximately 81,980 June and 81,980 December reviews and certifications that no changes have occurred (a total of 163,960 submissions annually).

The estimates for the number of drug listings submitted by manufacturers, repackers, relabelers, and drug product salvagers include both domestic and foreign listings and the listings that would be submitted by manufacturers, repackers, relabelers, and drug product salvagers for private label distributors. The estimates also include the time for submitting information for an NDC number under proposed § 207.33. The drugs that would be listed include PET drugs, an additional 57 drugs listed by approximately 5 foreign establishments as a result of the revocation of the exemptions for foreign establishments, and approximately 30 plasma derivatives. The estimates for the number of June and December reviews and updates of listing information or reviews and certifications that no changes have occurred would include the number of changes to drug characteristics submitted to obtain a new NDC number under proposed § 207.33(f) and the reports of the withdrawal of an approved drug from sale under § 314.81(b)(3)(iii) and, for biological products, under § 601.2(f).

Based on our familiarity with the content of current listing forms and submissions and the time required to input listing information during our electronic drug registration and listing system pilot project, we estimate that it will take manufacturers, repackers, relabelers, and drug product salvagers approximately 1 hour and 30 minutes to provide electronically information for each

drug they list for the first time (for both foreign and domestic listings). This estimate is 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. This estimate includes the time for submitting the content of labeling in electronic format under proposed § 207.61(a)(2) and for submitting other labeling and advertisements in paper or electronic format under proposed §§ 207.49(g) and (h) and 207.53(d) and (e). This estimate is only until manufacturers, repackers, relabelers, and drug product salvagers become familiar with using the electronic drug registration and listing system. We intend to lower this burden estimate to approximately 45 minutes when we submit to OMB the request to renew approval of this information collection.

We also estimate that it will take approximately 30 minutes for each June and December review and update of listing information, and approximately 15 minutes for each review and certification that no changes have occurred. These estimates include the time for submitting any labeling and advertisements for each drug, changes to the drug's characteristics submitted for a new NDC number under proposed § 207.33(f), and reports of the withdrawal of an approved drug from sale under § 314.81(b)(3)(iii). This estimate is only until manufacturers, repackers, relabelers, and drug product salvagers become familiar with using the electronic drug registration

and listing system. We intend to lower this burden estimate to approximately 15 minutes for each review and update and approximately 5 minutes for each review and certification when we submit to OMB the request to renew approval of this information collection. We note that these estimates for the electronic submission of this information would be a reduction in the currently approved estimate of 2.50 hours (OMB Control Number 0910-0045) for preparing and mailing to FDA Form FDA 2657 and FDA Form FDA 2658.

We intend to migrate into our new electronic drug registration and listing system current listing information that had been submitted using paper forms. As a result, current manufacturers, repackers, relabelers, and drug product salvagers will need additional time to review all current listing information in the new database and make any necessary revisions. We estimate that it will take on average 45 minutes to review and update each drug's listing information (the listing information includes information submitted for an NDC number).

Registration and Listing Information Under Proposed Part 607 - Burden Estimates

Based on the number of new establishments that currently register with FDA each year, we estimate that approximately 15 foreign establishments would provide new establishment registrations annually. Based on the number of registered establishments in our

database, we estimate that approximately 21 foreign establishments would provide approximately 105 annual reviews and updates of registration information or reviews and certifications that no changes have occurred. Based on the number of changes to registration information that have been submitted annually on Form FDA 2830, we estimate that approximately 21 foreign establishments would provide approximately 80 product listing updates.

The estimates above include 10 foreign establishments with blood products that enter a foreign trade zone and are re-exported from that foreign trade zone without having entered U.S. commerce under section 801(d)(4) of the act.

We estimate that it would take approximately 60 minutes to provide the initial registration and listing information for each new establishment.

We estimate that it would take approximately 30 minutes for each annual review and update of registration and listing information, including each review and certification that no changes have occurred.

We estimate that it would take approximately 15 minutes to provide the product listing update for each establishment.

The burden hour estimates above are based on institutional experience with the current registration and listing requirements. The estimates are an average of the time it would take to register a

foreign establishment and an average of the time it would take to review registration and listing information and update several registration and listing items in the database or review information and only certify that no changes have occurred.

Registration and Listing Information Under Proposed Part 1271 - Burden Estimates

Based on the number of new establishments that currently register with FDA each year, we estimate that approximately 300 establishments would provide new establishment registration annually. Based on information from FDA's database, we estimate that approximately 2,000 establishments are registered and listed with FDA. The number of establishments that currently register and list with FDA include both foreign and domestic establishments. Based on information from FDA's database, we estimate that approximately 1,400 establishments would provide establishment and listing updates. If no change has occurred, an update is not required. Based on the number of establishments from FDA's database, we estimate that approximately 1,800 establishments would provide approximately 2,100 changes to establishment ownership or location, or changes to the U.S. agent's information.

We estimate that it would take approximately 45 minutes to provide the initial registration and listing information for each new establishment.

We estimate that it would take approximately 30 minutes for each annual review and update of registration and listing information for each establishment.

We estimate that it would take approximately 15 minutes for each establishment to provide a change in ownership and location, or a change to the U.S. agent’s information.

The burden hour estimates above are based on institutional experience with the current registration and listing requirements. The estimates are an average of the time it would take to register an establishment, and an average of the time it would take to review registration and listing information, and update several registration and listing items in the database.

User Account Information for Electronic System

We estimate that approximately 8,343 manufacturers, repackers, relabelers, and drug product salvagers will provide this information (approximately 8,343 submissions) and that it will take approximately 15 minutes to provide the requested information.

Waiver Request Information - Part 207

We estimate that approximately two manufacturers, repackers, relabelers, or drug product salvagers would request a waiver annually, and that each request would take approximately 1 hour to prepare and submit to us.

In those instances when we grant a request for a waiver, we intend to make available to the manufacturer, repacker, relabeler, or drug product salvager paper forms -- revised Form FDA 2656 for registration and revised Form FDA 2657 for listing (the listing form would include a section for submitting the information required to obtain an NDC number). We intend to request public comment and OMB approval for the revised forms before the effective date of any final rule. The proposed form will be available from the Division of Compliance Risk Management and Surveillance, Office of Compliance, Center for Drug Evaluation and Research (HFD-330), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Waiver Request Information - Part 607

We estimate that approximately two manufacturers would request a waiver annually, and that each request would take approximately 1 hour to prepare and submit to us.

In those instances when we grant a request for a waiver, we intend to make available to the manufacturer the paper form -- Form FDA 2830 for registration and listing.

Waiver Request Information - Part 1271

We estimate that approximately 100 manufacturers would request a waiver annually, and that each request would take approximately 1 hour to prepare and submit to FDA.

In those instances when we grant a request for a waiver, we

intend to make available to the manufacturer the paper form -- revised Form FDA 3356 for registration and listing. We intend to request public comment and OMB approval for the revised form before the effective date of any final rule.

Public Disclosure Exemption Requests

Based on our experience with registration and listing information inspection requests under current § 207.37, we estimate that approximately 100 manufacturers, repackers, relabelers, or drug product salvagers would submit this request annually, and that each request would take approximately 1 hour to prepare and submit to us.

Revised Labeling Submitted With Annual Report

When there is a change in the NDC number on a drug label, or when an NDC number is added to a label, application holders must submit revised labeling to us with their annual reports under § 314.81(b)(2) for human drugs, § 514.80(b)(4) for animal drugs ("periodic reports" are required instead of "annual reports"), and § 601.12(f)(3) for biological drugs. The submission of annual reports (or periodic reports for animal drugs) under these regulations is already approved by OMB under Control Number 0910-0001 for human drugs (approval expires 5/31/08), Control Number 0910-0012 for animal drugs (approval expires 6/30/06), and Control Number 0910-0338 for biological products (approval expires 9/30/08). There would be no additional information collection burden associated with any

labeling revision because of a new NDC number assigned by us because it would be "public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public" and exempt under the PRA (5 CFR 1320.3(c)(2)). However, we have estimated a burden of approximately 5 minutes per annual report as the time required to state in the annual report that the labeling has been revised to include a new NDC number and the additional time required to submit to us the revised labeling with the annual report. For the number of submissions, we estimated that no more than approximately one-half of all annual reports submitted for products already listed with FDA on the effective date of the final rule would include this information.

FDA specifically requests comments on the burden hour estimates described above and in tables 1, 2, and 3 of this document.

Table 1.--ESTIMATED ANNUAL REPORTING BURDEN UNDER PROPOSED PART 207

21 CFR Sections and Reporting Requirements	Number of Respondents	Number of Responses Per Respondent	Total Annual Responses	Hours Per Registra-tion and Listing	Total Hours
Initial Establishment Registration (207.25)	987	1.14	1,128	1 hour	1,128
Annual Review and Update of Registration Information (207.29)	8,343	1.45	12,137	.50 hours	6,068.5
Expedited Updates (207.29)	775	2.46	1,921	.25 hours	480.25
Initial Listing and NDC Number Information (207.33, 207.49, 207.53, 207.54, 207.55)	1,812	7.63	13,821	1.50 hrs.	20,731.50
Review and Update of Listing					

Information (June and December) (207.33,207.37,207.57, 314.81(b)(3)(iii), 601.2(f)) Review and Certification of Listing Information (June and December) (207.57, 601.2(f))	2,278 5,594	19.81 29.29	45,136 163,960	.50 hours .25 hours	22,568 40,990
Review of registration information already in FDA database on effective date of final rule	8,343	1.45	12,137	.50 hours	6,068.5
Review of listing information already in FDA database on effective date of final rule	7,962	13.13	104,548	.75 hours	78,411
User accounts for electronic system	8,343	1	8,343	.25 hours	2,085.75
Waiver requests(207.65) Revised Forms FDA 2656 and 2657	2	1	2	1 hour	2
Public disclosure exemption requests (207.81(c))	100	1	100	1 hour	100
Annual report revision for new NDC number (314.81(b)(2); 514.80(b)(4); 601.12 (f)(3))	3,981	13.13	52,289	5 minutes	871.5
Total Reporting Burden					**179,505**

Table 2.--ESTIMATED ANNUAL REPORTING BURDEN UNDER PROPOSED PART 607

21 CFR Sections	Number of Respondents	Number of Responses Per Respondent	Total Annual Responses	Hours Per Registration and Listing	Total Hours
Initial Establishment Registration and Blood Product Listing (607.40)	15	1	15	1	15

Annual Review and Update of Establishment Registration and Blood Product Listing (607.40))	21	5	105	0.5	52.5
Product Listing Update (607.40)	21	3.8	80	0.25	20
Waiver requests (607.40(f)(1)) Revised Form FDA 2830	2	1	2	1	2
Total Reporting Burden					**89.5**

Table 3.--ESTIMATED ANNUAL REPORTING BURDEN UNDER PROPOSED PART 1271

21 CFR Sections	Number of Respondents	Number of Responses Per Respondent	Total Annual Responses	Hours Per Registration and Listing	Total Hours
Initial Establishment Registration and Listing (1271.25)	300	1	300	0.75	225
Annual Review and Update of Establishment Registration and Listing (1271.25)	2,000	1.4	1,400	0.5	501.5
Waiver requests (1271.23) Revised Form FDA 3356	100	1	100	1	100
Amend Establishment Registration (1271.26)	1800	1.16	2100	0.25	525
Total Reporting Burden					**1550.5**

13. Estimates of Annualized Cost Burden to Respondents

Based on an industry hourly wage average cost of $50 per hour, the annual cost is as follows: Total burden hours of 181,145 @ $50 per hour equals $9,057,250.

Table 4 shows the initial investment costs of the proposed rule (capital costs).

Cost Category	Initial Investment/One Time
Single Method of Assigning NDC Numbers	$3.8
Electronic Drug Registration and Listing	$0.2
Label Revisions	$36.2
Software Acquisition and Training	$1.3

These costs are discussed in detail in section VI (Analysis of Economic Impacts) of the proposed rule.

14. Estimates of Annualized Cost Burden to the 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 $250,000, the total cost to the government is approximately $ 7,500,000.

15. Changes in Burden

This request for OMB approval is for a proposed rule.

16. Time Schedule, Publication, and Analysis Plans

No comprehensive tabulation of the data is planned or anticipated.

17. Displaying of OMB Expiration Date

The FDA Forms involved in this collection will display the OMB expiration date.

18. Exception to the Certification Statement - Item 19

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 -

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

a. [x] New Collection

b. [ ] Revision of a currently approved collection

c. [] 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 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 – Proposed Rule

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

9. Keywords human drugs registration drugs

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 – 10,364 _____

b. Total annual responses – 419,624 _____

1. Percentage of these responses collected electronically – 100%

c. Total annual hours requested – 181,145 _____

d. Current OMB inventory – none; This is a proposed rule___

e. Difference _____

f. Explanation of difference

1. Program change _____

2. Adjustment _____

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

a. Total annualized capital/startup costs 41.5 million

b. Total annual costs (O&M) 0

c. Total annualized cost requested 41.5 million

d. Current OMB inventory 0

e. Difference 41.5 million

f. Explanation of difference This is a proposed rule___

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: Karen Nelson

	Phone: _____

praedrls.ss.doc 8/7/06; 9/6/06