OMB INFORMATION COLLECTION
SUPPORTING STATEMENT
0910-0338

Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use - Form FDA 356h

JUSTIFICATION

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting an extension of OMB Control No. 0910-0338 and OMB approval of Form FDA 356h - Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use, and the following information collection requirements in 21 CFR 601.2 (Tab A):

21 CFR 601.2	Reporting	Specifies procedures and requirements for filing for a biologics license application.

Statutory authority for the collection of this information is provided by sections 505(a), (b), and (j) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(a), (b), and (j)) (Tab B), and section 351 of the Public Health Service Act (PHS Act) (42 U.S.C. 262) (Tab C). Manufacturers of new drugs for human use regulated under the act must submit a new drug application (NDA) for review and approval to the Center for Biologics Evaluation and Research (CBER) or the Center for Drug Evaluation and Research (CDER) prior to marketing a drug in interstate commerce (21 CFR 314.50). Manufacturers of generic drugs regulated under the act must submit an abbreviated new drug application (ANDA) for review and approval to CDER prior to marketing a generic drug in interstate commerce (21 CFR 314.94). Manufacturers of biological products regulated under the PHS Act must submit an establishment license application (ELA) and a product license application (PLA) or biologics license application (BLA) for review and approval to CBER prior to marketing a biological product in interstate commerce (21 CFR 601.2). Blood and blood components fall within the category of biological products. All establishments collecting and/or preparing blood and blood components for sale or distribution in interstate commerce are subject to the licensing application provisions of section 351 of the PHS Act. Applicants are required to report to FDA any transfer of ownership of an NDA (21 CFR 314.72). Applicants are required to report a change in ownership of an ANDA (21 CFR 314.99(a)). Manufacturers of a drug or biologic for human use are required to file supplemental applications for certain changes to applications previously approved (21 CFR 314.70, 314.71, 314.97, and 601.12). The form is also submitted with an amendment to an unapproved original application or supplemental application, and a presubmission or resubmission of information pertaining to an application.

The information provided by manufacturers with the application form is necessary for FDA to carry out its mission of protecting the public health and helping to ensure that drugs and biologics for human use have been shown to be safe and effective. Form FDA 356h was developed initially as a checklist to assist manufacturers in filling a drug application and has been previously used only by manufacturers of products regulated under the act. In the Federal Register of July 8, 1997 (62 FR 36558) (Tab D), FDA announced the availability of the revised Form FDA 356h. The form was revised as a "Reinventing Government" initiative to harmonize application procedures between CBER and CDER. The application form serves primarily as a checklist for firms to gather and submit to the agency studies and data that have been completed. The checklist helps to ensure that the application is complete and contains all the necessary information, so that delays due to lack of information may be eliminated. The

form provides key information to the agency for efficient handling and distribution to the appropriate staff for review. For biologics manufacturers, the form will replace a number of different ELA and PLA forms that were formerly used for these products. The information collection burden for various ELA and PLA forms is covered under OMB Control No. 0910-0124.

2. Purpose and Use of the Information

FDA is the Federal agency charged with responsibility for determining that drugs, including antibiotic drugs, and biologics are safe and effective. Manufacturers of a drug, or biologic for human use must file applications for FDA approval of the product prior to introducing it into interstate commerce. In addition, manufacturers are required to submit changes to an approved application. The information submitted to FDA in a biologics license application, new drug application, supplement to an approved application, or other similar submission is used to determine if a product is safe and effective.

Without this information, FDA could not monitor industry procedures and discharge its statutory responsibility for protecting the nation's health.

3. Use of Information Technology and Burden Reduction

One of FDA's continuing objectives is to improve the speed and quality of its review and approval programs. In order to reach a decision to approve an application, the agency must evaluate all information and data provided by applicants on the safety and efficacy of the proposed product. To make the review process more efficient for industry and FDA, CDER and CBER are utilizing electronic information systems technology.

In the mid-1980's, FDA began working with pharmaceutical sponsors to develop Computer-Assisted New Drug Applications (CANDA). CANDAs were designed to provide information (text, data, image) electronically to facilitate the review of applications. These efforts yielded valuable information but were limited because for each new drug review division sponsors tended to develop different hardware and software approaches. A reviewer might be confronted with an array of hardware, software, and review tools to conduct a review that differed among sponsors and applications. Also, CANDAs were never approved as a substitute for the archival copy, so firms were still required to submit copies. One solution to limitations of CANDAs was an approach whereby staff responsible for a particular review discipline (eg, chemistry, clinical) worked directly with pharmaceutical sponsors to develop a consistent approach that would be applicable to all sponsors and to all review divisions. Focus on this approach has evolved into the Electronic Regulatory Submission and Review (ERSR) Program. This new initiative is intended to ensure both the electronic availability of information and the means to manipulate this information electronically to yield a review. ERSR is made up of a variety of projects that are in different stages of development and implementation. These projects are categorized into 3 areas: First, "Electronic Submissions" includes standards-related projects to define the format and content of regulatory submissions; written guidance for industry to follow in preparing electronic submissions; an Electronic Document Room project to accommodate the receipt, archive, and storage of electronic transmissions; an Electronic Gateway project to provide an agency-level central point for receipt of secure electronic transmissions and routing to the Centers; and scientific databases that include structured databases, reference guides, and analytical tools used by reviewers. Second, "Corporate Databases, Document bases and Applications" includes projects under the Electronic Document Management System and the Management Information System. Third, other electronic initiatives including technical infrastructure, technical support, and training. CDER has issued the Guidance for

Industry documents entitled "Regulatory Submissions in Electronic Format - NDAs" and "Regulatory Submissions in Electronic Format - General Considerations".

CBER is now accepting electronic BLAs and has recently issued guidance to assist manufacturers in this area ("Guidance for Industry: Electronic Submissions of a Biologics License Application (BLA) or Product License Application (PLA)/Establishment License Application (ELA) to the Center for Biologics Evaluation and Research").

FDA believes the increased use of computer assisted license applications will enhance the timeliness, effectiveness, and efficiency of the review process and reduce burdensome, nonessential hard-copy handling and storage. FDA is not aware of any other improved technology to reduce the burden.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only agency that requires the filing of an application for the marketing of a new drug or biological product for human use. No other component of the agency or other government agencies require similar information or data to be filed. This information is not available from any other source.

5. Impact on Small Businesses or Other Small Entities

FDA believes that its duty requires the equal application of the regulations to all enterprises. While FDA does not believe it can apply different standards with respect to statutory requirements, FDA does provide special help to small businesses. CBER's Office of Communication, Training, and Manufacturer's Assistance, and CDER's Office of Training and Communications provide assistance to small businesses subject to FDA's regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

Manufacturers are required to submit applications for approval of a new drug or biological product prior to marketing such products in interstate commerce. Manufacturers are required to submit a supplement to an approved an application prior to implementing a change or in an annual report depending on the significance of the change. Less frequent collection of information will not provide the necessary information needed by FDA to properly evaluate the safety and effectiveness of a new drug or biological product.

There are no technical or legal obstacles to reducing the burden.

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

An applicant may be required to submit to FDA proprietary trade secret or other confidential information when submitting a BLA, NDA, or other similar submission. FDA has instituted security measures to protect confidential information received from manufacturers and will, to the extent permitted by law, protect the information.

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

In accordance with 5 CFR 1320.8(d), a 60-day notice for public comment on the information collection

provisions was published in the **Federal Register** of October 21, 1999 (64 FR 56797) (Tab E). No comments were received from the public.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift was provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

The confidentiality of information received by FDA would be consistent with the Freedom of Information Act and the agency's regulations under 21 CFR Part 20, § 314.430, and § 601.51. Manufacturers submitting an application for FDA approval to market a new drug or biological product in interstate commerce, or other similar submission may be required to include proprietary or trade information. However, such proprietary or trade information is deleted from any information released by FDA under the Freedom of Information Act and FDA regulations.

11. Justification for Sensitive Questions

Questions of a sensitive nature are not applicable to this information collection.

12. Estimates of Hour Burden Including Annualized Hourly Costs

The estimated annual burden for this information collection is 602,856 hours.

TABLE 1. - Estimated Annual Reporting Burden for Biologics

21 CFR Part/FDA Form	No. of Respondents	Total Annual Response	Hours per Response	Total Hours
601.2	343	84	1,600	134,400
Form 356h	343	4,947	16	79,152
Total				213,552

There are an estimated 343 licensed biologics manufacturers. However, not all manufacturers will have any submissions in a given year and some may have multiple submissions. The annual responses are based on submissions received by FDA in 1998. The rate of submissions are not expected to change significantly in the next few years. The time estimated to prepare an ELA/PLA or BLA under §601.2 for CBER approval to market a new product is based on information provided by industry. The time required for preparing an ELA/PLA or BLA includes the estimate for filling out the form. The estimated average burden hours for the other submissions using Form 356h to CBER is based on past FDA experience and includes the time to fill out the form and collate the documentation. The average burden hours also include the time to prepare an amendment submitted to CBER. The estimated burden hours to prepare a supplement to CBER (§601.12) are reported under 0910-0315.

TABLE 2. - Estimated Annual Reporting Burden for Human Drugs

21 CFR Part/FDA Form	No. of Respondents	Total Annual Response	Hours per Response	Total Hours
Form 356h	483	16,221	24	389,304
Total				389,304

There are 483 drug applicants that submitted the form. The annual responses are based on submissions received by FDA in 1997 and 1998. The rate of submissions are not expected to change significantly in the next few years. The estimated average burden hours for the submissions using Form 356h to CDER is based on past FDA experience and includes the time to fill out the form and collate the documentation. The estimated burden hours to prepare an NDA (21 CFR 314.50); an ANDA (21 CFR 314.94); supplements (21 CFR 314.70, 314.71, and 314.97); and amendments (21 CFR 314.60 and 314.96) are approved under OMB Control No. 0910-0001.

Cost to Respondents

The estimated annual cost to respondents is $1,878,964.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	602,856	$35.00	$21,099,960

The cost estimate is based on a regulatory affairs specialist, at a pay rate of $35.00/hour, who would be responsible for filling out the form, and preparing an application, supplement, or other similar submission.

13. Estimate of Other Total Annual Cost Burden to Respondents or Record-keepers

There are no capital and start-up, or operation, maintenance and purchase costs associated with the collection of information requirements.

14. Annualized Costs to the Federal Government

The estimated annualized cost to the Federal Government is $34,109,598.00. This estimate is based on full-time equivalents (FTEs) associated with the review of applications including supplemental applications and other similar submissions, and the average annual salaries for CBER and CDER reviewers.

The amount of time and expense incurred by the Federal government is due to the review of all material submitted with an application and other similar submissions. This information is essential to determine the safety and effectiveness of products in support of FDA's mission to protect the public health. This information may include clinical data, safety updates, samples submitted for evaluation by the agency, case report tabulations, case report forms, and patient information.

Activity	Number of FTEs	Average Annual Reviewer Salary	Total Cost
Application Review/CBER	168	$65.160.00	$23,162,718.00
Application Review/CDER	327	$70,834.00	$10,946,880.00
Total			$34,109,598.00

15. Explanation of Program Changes or Adjustments

The estimated total annual burden for this information collection requirements was 485, 480 hours in 1997. The increase in burden is mostly attributed to the addition of § 601.2 to this information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no tabulated results to publish for this information collection.

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

FDA is not seeking approval to exempt display of the expiration date for OMB approval.

18. Exception to Certification for Paperwork Reduction Act Submissions

There are no exceptions to Item 19 of OMB Form 83-I.