Request for Samples and Protocols

0910-0206

SUPPORTING STATEMENT

Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting an extension of Office of Management and Budget (OMB) Control No. 0910-0206 and OMB approval of the information collection requirements for the regulations listed below.

21 CFR 610.2	Reporting	The Center for Biologics Evaluation and Research (CBER) and the Center for Drugs Evaluation and Research (CDER) may at any time require manufacturers of licensed biological products to submit to FDA samples of any lot along with the protocols showing the results of applicable tests prior to distributing the lot of the product.
21 CFR 660.6(b)	Reporting	Along with each required sample, FDA requires the manufacturer to submit a protocol that consists of a summary of the history of manufacture of the product including all results of each test for which test results are requested by CBER.
21 CFR 660.36(a)(2) and (b)	Reporting	Section 660.36(a)(2) requires that a protocol contain information including, but not limited to, manufacturing records, test records, and test results. Section 660.36 (b) requires that a copy of the antigenic constitution matrix specifying the antigens present or absent be submitted to the CBER Director at the time of initial distribution of each lot.
21 CFR 660.46(b)	Reporting	Along with each required sample, FDA requires the manufacturer to submit a protocol that consists of a summary of the history of manufacture of the product including all results of each test for which test results are requested by CBER.

Under section 351 of the Public Health Service Act (the PHS Act)(42 U.S.C. 262), FDA has the responsibility to issue regulations that prescribe standards designed to ensure the safety, purity, and potency of biological products and to ensure that biologics licenses for such

products are only issued when a product meets the prescribed standards. Samples and protocols are required by FDA to help ensure the safety, purity, and potency of a product because of the potential lot-to-lot variability of a product produced from living organisms. In addition to § 610.2 (21 CFR 610.2), there are other regulations that require the submission of samples and protocols for specific licensed biological products: §§ 660.6 (21 CFR 660.6) (Antibody to Hepatitis B Surface Antigen); 660.36 (21 CFR 660.36) (Reagent Red Blood Cells); and 660.46 (21 CFR 660.46) (Hepatitis B Surface Antigen). In cases of certain biological products (e.g., Albumin, Plasma Protein Fraction, and therapeutic biological products) that are known to have lot-to-lot consistency, official lot release is not normally required. However, submissions of samples and protocols of these products may still be required for surveillance, licensing, and export purposes, or in the event that FDA obtains information that the manufacturing process may not result in consistent product quality.

2. Purpose and Use of the Information Collection

Samples and protocols are required to be submitted to FDA. The written protocols are reviewed by FDA scientists and other staff with expertise in the appropriate product and scientific area. FDA tests samples to verify the manufacturer's test results. A manufacturer may not distribute a product until FDA gives the official release for the lot.

3. Use of Improved Information Technology and Burden Reduction

One of FDA's continuing objectives is to improve the speed and quality of its review and approval programs. CBER intends to continue this trend by accepting electronic lot release protocols and has issued guidance to assist manufacturers in this area. FDA believes that the increased use of computer-assisted protocol submissions 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 submission of samples and protocols for biological products for the purposes of lot release. No other government agencies require similar information or data to be submitted. This information is not available from any other source.

5. Impact on Small Businesses or Other Small Entities

Although FDA must apply the statutory and regulatory requirements equally to all enterprises, FDA does provide special help to small businesses. CBER's Office of Communication, Outreach, and Development, Division of Manufacturers Assistance and Training, and CDER's Office of Training and Communications provides assistance to small businesses subject to FDA's regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

Less frequent collection of information will not provide the information that FDA needs to properly evaluate results of specific tests identified for lot release review in the license application.

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 protocol. FDA has security measures to protect confidential information received from manufacturers and will, to the extent permitted by law, protect the information. In addition, the frequency of submissions may be more often than quarterly depending on the number of lots produced for a product over that time.

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

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice in the *Federal Register* on March 6, 2009 (74 FR 9820), for public comment on the information collection provisions.

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 FDA's regulations under 21 CFR Part 20. Proprietary or trade secret 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 Annualized Burden Hours and Costs

The total annual estimated burden for this collection of information is 19,155 hours.

Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Response	Hours per Response	Total Hours
610.2	65	95.5	6,208	3	18,624
660.6(b)	2	44	88	5	440
660.36(a)(2) and (b)	1	1	1	6	6
660.46(b)	1	17	17	5	85
Total	69		6,314		19,155

The burden estimate is for protocols required to be submitted with each sample. The collection of samples is not a collection of information under 5 CFR 1320.3(h)(2). Respondents to the collection of information under § 610.2 are manufacturers of licensed biological products. Respondents to the collection of information under §§ 660.6(b), 660.36(a)(2) and (b), and 660.46(b) are manufacturers of the specific products under these regulations. The estimated number of respondents for each regulation is based on the annual number of manufacturers that submitted samples and protocols for biological products, including submissions for lot release, surveillance, licensing, or export. Based on information obtained from FDA's database system, approximately 69 manufacturers submitted samples and protocols in fiscal year 2008 under the regulations cited above. FDA estimates that approximately 65 manufacturers submitted protocols under § 610.2, and 4 manufacturers submitted protocols under the regulations for the specific products. FDA received no submissions under § 660.36, however FDA is using the estimate of one protocol submission in the event one is submitted in the future.

The estimated total annual responses are based on FDA's final actions completed in fiscal year 2008, which totaled 6,314, for the various submission requirements of samples and protocols for licensed biological products. The rate of final actions is not expected to change significantly in the next few years. The hours per response are based on information provided by industry. The burden estimates provided by industry ranged from 1 to 5.5 hours. Under § 610.2, the hours per response are based on the average of these estimates and rounded to 3 hours. Under the remaining regulations, the hours per response are based on the higher end of the estimate (rounded to 5 or 6 hours) because more information is generally required to be submitted in the protocol than under § 610.2.

Cost to Respondents

The estimated annual cost to respondents is $1,110,990.00.

Activity	No. of Hours	Cost per Hour	Total Cost
Reporting	19,155	$58.00	$1,110,990.00

The cost estimate is based on an average pay rate of $58.00/hour. This average is based on the salaries of an upper-level manager, mid-level professional, and clerical support that may be involved in the preparation and submission of the protocol.

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

There are no capital or operating, and maintenance costs associated with this collection.

14. Annualized Cost to Federal Government

The estimated annualized cost to FDA is $871,332.00. The review of each protocol by FDA involves approximately six persons, at an average pay rate of $46.00/hour, who spend a total of approximately 3 hours per protocol. The estimate is based on FDA's final actions completed in fiscal year 2008, which totaled 6,314. This estimate does not include the time related to the testing of samples, because the submission of samples is not a collection of information.

Activity	Number of Reviews	Review Time	Average Cost per Hour	Total Cost
Protocol Review	6,314	3 hrs.	$46.00	$871,332.00

15. Explanation for Program Changes or Adjustments

The previous burden estimate was 15,019 hours. The current burden estimate is 19,155 hours. This adjustment in burden (+4,136 hours) is due to an increase in the number of submissions under § 610.2.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no results to publish for this information collection.

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

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

18. Exceptions to Certification for Paperwork Reduction Act Submissions

N/A