Supporting Statement for
CERTIFICATION TO ACCOMPANY DRUG, BIOLOGICAL PRODUCT, AND DEVICE APPLICATIONS/SUBMISSIONS

OMB Control No. 0910-0616

A. Justification

1. Circumstances Making the Collection of Information Necessary

Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA), Public Law 110-85, amended the Public Health Service Act (PHS Act) by adding section 402(j), 42 U.S.C. § 282(j). The provisions require additional information to be submitted to the clinical trials data bank (ClinicalTrials.gov) previously established by the National Institutes of Health/National Library of Medicine (NIH/NLM), including expanded information on clinical trials and information on the results of clinical trials. The provisions include responsibilities for the Food and Drug Administration (FDA) as well as several amendments to the Federal Food, Drug, and Cosmetic Act (FD&C Act).

One provision, 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, requires that a certification accompany human drug, biological, and device product submissions made to FDA. Specifically, at the time of submission of an application under sections 505, 515, or 520(m) of the FD&C Act, or under section 351 of the PHS Act, or submission of a report under section 510(k) of the FD&C Act, such application or submission must be accompanied by a certification that all applicable requirements of section 402(j) have been met. Where available, such certification must include the appropriate National Clinical Trial (NCT) numbers.

The importance of obtaining these data relates to adherence to the legal requirements for submissions to the clinical trials registry and results data bank and ensuring that individuals and organizations submitting applications or reports to FDA under the listed provisions of the FD&C Act or the PHS Act adhere to the appropriate legal and regulatory requirements for certifying to having complied with those requirements. The failure to submit the certification required by 42 U.S.C. 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, and the knowing submission of a false certification are both prohibited acts under section 301 of the FD&C Act. Violations are subject to civil money penalties.

2. Purpose and Use of the Information Collection

The collection of information required under 42 U.S.C. 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, can be submitted electronically or manually to FDA.

This information will be submitted to FDA with new investigational and marketing applications/submissions and certain additional submissions to such applications for human drugs, biological products, and devices. It will be used to confirm that sponsors/applicants/submitters have complied with the certification provisions in the law with regard to any applicable clinical trials referenced in the investigational or marketing

applications/submissions with which the certification is submitted. The information also will provide a means of correlating the clinical trials contained in the applications/submissions to FDA with the information contained in the ClinicalTrials.gov data bank.

3. Use of Improved Information Technology and Burden Reduction

The agency is not yet equipped to receive all investigational and marketing applications/submissions electronically; therefore, this reporting requirement will not mandate the use of automated, electronic, mechanical, or other technological collection techniques or other forms of information technology for this certification form. However, the form is designed to be able to be electronically completed and, if desired, electronically submitted by the applicant/submitter. Because the form will accompany an investigational or marketing application/submission, the form will be submitted in the same manner as the application/submission that it accompanies. There are Center-wide efforts to moving to e-submission of applications, and we are working very closely to include this certification form in those efforts.

4. Efforts to Identify Duplication and Use of Similar Information

The proposed information collection is not already available to FDA. Such information is only available from the individuals or entities responsible for submitting such information to the ClinicalTrials.gov data bank, or from the product applicants/submitters and product application/submission holders referenced in their applications/submissions. The information will vary for each drug, biological product, or device application/ submission. Only the submitter of the medical product application/submission has the ability to certify that the requirements of 42 U.S.C. § 282(j), section 402(j) PHS Act have been met or are not applicable to the clinical trials being referenced in the application/ submission being submitted to FDA.

FDA is the only agency that reviews, approves, and/or clears medical product applications/submissions (including investigational new drug applications (INDs), new drug applications (NDAs), abbreviated new drug applications (ANDAs) biologics license applications (BLAs), premarket notification (510(k)s), humanitarian device exemptions (HDEs), and premarket approval (PMAs)). We, thus, have not undertaken literature searches or contacted staff of other organizations with respect to this information collection.

5. Impact on Small Businesses or Other Small Entities

The reporting requirements of this statute are those mandated by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, as enacted by Title VIII, FDAAA. They will not be a burden to small businesses. However, FDA also aids small businesses in dealing with any requirements through the Office of Small Manufacturers Assistance and through the scientific and administrative staffs within the agency.

6. Consequences of Collecting the Information Less Frequently

The information is collected if a sponsor/applicant/submitter submits certain applications or reports to FDA under sections 505, 510(k), 515, or 520(m) of the FD&C Act or under section 351 of the PHS Act. If the collection is not conducted, or is conducted less frequently, the sponsor/applicant/submitter will not be in compliance with 42 U.S.C. 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act. In order to lessen the burden, we issued our January 2009 Guidance[1] which clarified which applications/submissions required certification; this guidance excluded annual reports and labeling supplements which reduces the burden. These changes are reflected in the revised tables.

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

This collection fully complies with 5 CFR 1320.5.

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 for public comment in the FEDERAL REGISTER on May 6, 2011 (76 FR 26305). There were four comments submitted in response to the 60-day Federal Register Notice. Only two comments were directly related to the information collection. One comment was unrelated to the information collection. The remaining comment requested that FDA define a term contained in 42 U.S.C. 282(j)(1)(A)(ii), section 402(j)(1)(A)(ii) of the PHS Act. The implementation of this provision, including defining any statutory terms, is the responsibility of NIH. NIH has indicated in the Unified Agenda that proposed rulemaking is anticipated in 2011. In addition, NIH has provided an elaboration of the definition of that term on its website at http://prsinfo.clinicaltrials.gov/ElaborationsOnDefinitions.pdf.

One of the comments which directly addressed the information collection commented on the utility of the information collected through Form FDA 3674 and requested that FDA consider a means to associate the NCT number with the study numbers. Since the enactment of FDAAA, FDA has been involved in a technological effort designed to accomplish what has been suggested by the comment. FDA is currently involved in designing a software/computer system that can link the information provided on the Form FDA 3674 with actions taken in relation to that study, a future marketing application, and future actions taken in relation to the approved medical product. Part of this effort is designed to provide NIH information which will be displayed on its website for each clinical trial for which specific information is provided. An additional aspect for the effort is designed to link this information internally for various purposes including compliance efforts. This commenter also proposed changes to the timing of the certification submissions accompanying INDs based upon the requirements for submission of clinical trial information to ClinicalTrials.gov. FDA appreciates the

[1] Guidance for Sponsors, Industry, Researchers, Investigators, and Food and Drug Administration Staff - Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of The Food and Drug Administration Amendments Act of 2007 (last revised March 5, 2009) available at http://www.fda.gov/RegulatoryInformation/Guidances/ucm125335.htm.

comment but has implemented the statutory requirements in the most efficient manner possible. The statute requires FDA to obtain the certification upon submission of an IND despite the fact that submission of clinical trial information to ClinicalTrials.gov generally is not required at the time an IND is required to be submitted. In order to collect information on trials that are not applicable clinical trials, as suggested by the comment, either a statutory change or, possibly, rulemaking would be required.

The remaining comment contended that the estimates FDA used in its burden estimates should be adjusted significantly upward. We do not agree with the comment's conclusions. FDA has based the burden hours on the totality of the time needed for the information collection and not (as claimed by the commenter) on the completion of the form itself. As noted in our previous information collection and this one, we anticipated that entities submitting Form FDA 3674 would implement systems that would simplify collection of the information. We have received feedback based on submitters' experience over the past three and one-half years that suggests these types of systems have been implemented. Furthermore, given the responsibilities required for registering and updating trials on ClinicalTrials.gov and current FDA requirements, unrelated to Form FDA 3674, for submission of trial information for marketing applications, the information required for completion of this form should be easy to compile. FDA's experience in responding to calls on the form and questions presented at meetings and conferences does not accord with the practices noted in this comment and does not support the burden estimates proposed by the comment. In fact the only other comment submitted directly related to the information collection indicated that the "estimate of the burden of the proposed collection of information, including the validity of the methodology and assumption used, seems reasonable."

9. Explanation of Any Payment or Gift to Respondents

No gifts or payments are to be offered in regard to this information collection.

10. Assurance of Confidentiality Provided to Respondents

All information received by FDA is subject to the confidentiality and privacy provisions in the Freedom of Information Act (5 U.S.C. § 552), the Privacy Act (5 U.S.C. § 552a), and the agency's regulations about public information (21 CFR Part 20).

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

The information required under 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act, will be submitted with applications/submissions currently submitted to FDA under 21 CFR part 312 and 314 (human drugs) approved under OMB control numbers 0910-0014 (expires August 31, 2011) and 0910-0001 (expires May 31, 2011), respectively, 21

CFR part 312 and 601 (biological products) approved under OMB control numbers 0910-0014 and 0910-0338 (expires June 30, 2010) and 21 CFR parts 807 and 814 (devices) approved under OMB control numbers 0910-0120 (expires August 31, 2010) and 0910-0231 (expires December 31, 2013), respectively.

Table 1 below provides an estimate of the annual reporting burden for the submission of information from 2009 to 2010 to satisfy the requirements of 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the PHS Act. The annual reporting burden reflects a significant reduction in burden hours from the original estimates. These changes are made based on certain applications/submissions either removed from the burden calculations made in the original estimates or new applications/submissions added to the burden calculations. Those applications/submissions removed include those we currently have determined do not typically require that a certification form accompany the application/submission, as described in our January 2009 Guidance. Added to the burden were generic applications/submissions which were originally not included in the burden calculations, but have since been determined to require that a certification form accompany the application/submission.

Estimated Annual Reporting Burden				
	Investigational Applications	Marketing Applications	Hours per Response	Total Hours
CDER				
New Applications (IND)	1,752	----	.25	438
Clinical Protocol Amendments (IND)	11,769	----	.25	2,942
New Marketing Applications/Resubmissions (NDA/BLA)	----	157	.75	118
Clinical Amendments to Marketing Applications	----	1,466	.75	1,100
Efficacy Supplements/Resubmissions	----	166	.75	125
CBER				
New Applications (IND)	281	----	.25	70
Clinical Protocol Amendments (IND)	1,471	----	.25	368
New Marketing Applications/Resubmissions	----	8	.75	6
Clinical Amendments to Marketing Applications	----	17	.75	13
Efficacy Supplements/Resubmissions (BLA only)	----	25	.75	19
CDRH				
New Marketing Applications (includes PMAs, HDEs,	----	892	.75	669

Supplements and 510(k)s expected to contain clinical data)				
OGD				
Original Applications	----	854	.75	641
BE Supplements/Amendments	----	495	.75	372
Total				6,881

We believe the estimate of 6,888 hours per year accurately reflects the burden. We recognize that some individuals or entities less familiar with FDA forms and the clinical trials data bank (ClinicalTrials.gov) may require greater than 15 and 45 minutes (depending on the type of application/submission) per response. From our experience with current submissions, individual and entities (i.e. industry) have made completion and submission of the certification form part of their standard practice (i.e. part of their SOPs, retain electronic copies of submissions and simply update NCT numbers on subsequent forms). In addition we have participated in numerous conferences on the requirements and the form and have received positive feedback about the implementation of this activity.

We do not believe there is a new recordkeeping burden associated with the submission of this certification form. Current recordkeeping levels should be sufficient to complete and submit the certification form.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/ Capital Costs

There are no other total annual or capital costs to respondents.

14. Annualized Cost to the Federal Government

The estimated cost to the Federal Government for this information is not able to be specifically identified. The form is required to accompany other applications and submissions and is submitted as part of the entire package of documents.

15. Explanation for Program Changes or Adjustments

The decrease in burden (a program change) reflects changes made based on certain applications/submissions either removed from the burden calculations made in the original estimates or new applications/submissions added to the burden calculations. Those applications/submissions removed include those we currently have determined do not typically require that a certification form accompany the application/submission, as described in our January 2009 Guidance. In this guidance, we eliminated annual reports and labeling supplements from the list of applications/submissions that required a certification.

16. Plans for Tabulation and Publication and Project Time Schedule

The information collection requirements will not be published, tabulated, or manipulated.

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

No exemption is requested.

18. Exceptions to “Certification for Paperwork Reduction Act Submissions”

No exceptions are requested.

B. COLLECTION OF INFORMATION EMPLOYING STATISTICAL METHODS

This collection of information does not employ statistical methods.