Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees

0910-0581

SUPPORTING STATEMENT

Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting Office of Management and Budget (OMB) approval of the information collection provisions contained in a document entitled "Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees." The information collection provisions are listed below:

Sponsor notification to the DMC regarding waivers	Reporting	Recommends that sponsors notify DMCs about any waivers granted by FDA for expedited reporting of certain serious events.
DMC reports of meeting minutes to the sponsor	Reporting	Recommends that the DMC issue a written report to the sponsor based on the meeting minutes. Reports to the sponsor should include only those data generally available to the sponsor. The sponsor may convey the relevant information in this report to other interested parties such as study investigators.
Sponsor reporting to FDA on DMC recommendations related to safety	Reporting	Recommends that sponsors inform FDA about all recommendations related to the safety of the investigational product whether or not the adverse event in question meets the definition of "serious."
Standard Operating Procedures (SOPs) for DMCs	Recordkeeping	Recommends that sponsors establish certain procedures.
DMC meeting records	Recordkeeping	Recommends that the DMC or the group preparing the interim reports to the DMC maintain all meeting records.

Sponsors are required to monitor studies evaluating new drugs, biologics, and devices (21 CFR 312.50 and 312.56 for drugs and biologics, and 21 CFR 812.40 and 812.46 for devices). Various individuals and groups play different roles in clinical trial monitoring. One such group is a Data Monitoring Committee (DMC), appointed by a sponsor to evaluate the accumulating outcome data in some trials. A clinical trial DMC is a group of individuals with pertinent expertise that reviews on a regular basis accumulating data from an ongoing clinical trial. The DMC advises the sponsor regarding the continuing safety of current participants and those yet to be recruited, as well as the continuing validity and scientific merit of the trial.

The guidance document is intended to assist sponsors of clinical trials in determining when a DMC is needed for study monitoring, and how such committees should operate. The guidance addresses the roles, responsibilities, and operating procedures of DMCs.

2. Purpose and Use of the Information Collection

The submission of the requested information provides the appropriate parties with essential information regarding the trial upon which they may base their recommendations. The SOPs ensure that established written procedures are followed.

3. Use of Improved Information Technology and Burden Reduction

Manufacturers may use computers, tapes, microfiche, or microfilm in lieu of hard copy records. 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 requests this information. There is no similar kind of information available from any other source.

5. Impact on Small Businesses or Other Small Entities

While FDA does not believe it can apply different standards with respect to regulatory and statutory requirements, FDA does provide special help to small businesses. The Center for Biologics Evaluation and Research (CBER), Office of Communications, Training, and Manufacturers Assistance, the Center for Drug Evaluation and Research (CDER), Office of Training and Communications, and the Center for Devices and Radiological Health (CDRH), Division of Small Manufacturers, International and Consumer Assistance provide assistance to small businesses subject to FDA's regulatory requirements.

6. Consequences of Collecting the Information Less Frequently

Less frequent collection of information or other methods of reducing the frequency of information would not provide the information needed by FDA or the DMC to evaluate the submitted information. There are no technical or legal obstacles to reducing the burden.

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

There is no special circumstance for the collection of the information requirements.

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 notice in the FEDERAL REGISTER of October 8, 2008 (73 FR 58970), providing for a 60-day comment period on the information collection. No comments were received in response to the notice.

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 is consistent with the Freedom of Information Act and the agency's regulations under 21 CFR Part 20.

11. Justification for Sensitive Questions

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

12. Estimates of Annualized Burden Hours and Cost

The total estimated burden for both the reporting and recordkeeping burdens under the guidance are 1,794.75 hours.

Table 1--Estimated Annual Reporting Burden					
Section of Guidance/Reporting Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
4.4.1.2. Sponsor notification to the DMC regarding waivers	1	1	1	.25	.25
4.4.3.2. DMC reports of meeting minutes to the sponsor	370	2	740	1	740
5. Sponsor reporting to FDA on DMC recommendations related to safety	37	1	37	.5	18.50
Total					758.75

Table 2--Estimated Annual Recordkeeping Burden					
Recordkeeping Activity	No. of Record-keepers	Annual Frequency per Record	Total Annual Records	Hours per Record-keeper	Total Hours
4.1. and 6.4 SOPs for DMCs	37	1	37	8	296
4.4.3.2. DMC meeting records	370	1	370	2	740
Total					1,036

Based on information from FDA review divisions, FDA estimates there are approximately 740 clinical trials with DMCs regulated by CBER, CDER, and CDRH. FDA estimates that the average length of a clinical trial is two years, resulting in an annual estimate of 370 clinical trials. Because FDA has no information on which to project a change in the use of DMCs, FDA estimates that the number of clinical trials with DMCs will not change significantly in the next few years. For purposes of this information collection, FDA estimates that each sponsor is responsible for approximately 10 trials, resulting in an estimated 37 sponsors that would be affected by the guidance annually.

Based on information provided to FDA by sponsors that have typically used DMCs for the kinds of studies for which this guidance recommends them, FDA estimates that the majority of sponsors have already prepared SOPs for DMCs, and only a minimum amount of time would be necessary to revise or update them for use for other clinical studies. FDA receives very few requests for waivers regarding expedited reporting of certain serious events, therefore, FDA has estimated one respondent per year to account for the rare instance a request may be made. FDA estimates that the DMCs would hold two meetings per year per clinical trial resulting in the issuance of two DMC reports of the meeting minutes to the sponsor. One set of both of the meeting records should be maintained per clinical trial.

The hours per response and hours per record are based on FDA's experience with comparable recordkeeping and reporting provisions applicable to FDA regulated industry. The hours per response include the time the respondent would spend reviewing, gathering, and preparing the information to be submitted to the DMC, FDA, or the sponsor. The hours per record include the time to record, gather, and maintain the information.

Cost to Respondents

Activity	No. of Hours	Cost per hour	Total Cost
Reporting	18.75	$47.00	$881.00
Reporting	740	$78.00	$57,720.00
Recordkeeping	296	$47.00	$13,912.00
Recordkeeping	740	$78.00	$57,720.00
Total			$130,233.00

The annual cost to the respondents is estimated at $130,233.00. The cost is based on a regulatory affairs specialist ($47/hr) who would be responsible for preparing and submitting the appropriate information to FDA or the DMC, and maintaining the SOPs; and the DMC Chair ($78/hr) who would be responsible for issuing a report to the sponsor, and maintaining the records. The salary estimate includes benefits but no overhead costs.

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

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

14. Annualized Cost to the Federal Government

The estimated annualized cost to the Federal Government is $27,084. The estimate includes the average numbers of hours by FDA to review the safety-related recommendations. The estimated cost is based on an average grade scale of a GS-14 ($61/hour) reviewer. The salary estimate includes benefits but no overhead costs.

Activity	Number of Responses	Hours per Response	Cost per Hour	Total Cost
Review	37	12	$61.00	$27,084.00

15. Explanation for Program Changes or Adjustments

There are no program changes or adjustments from the previous submission.

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 the display of the expiration date of the OMB approval.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

N/A.