

SUPPORTING STATEMENT  
OMB Control No. 0910-0581

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

**JUSTIFICATION**

1. Need and Legal Basis

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” (Tab A). The information collection provisions are listed below:

Sponsor notification to the DMC regarding waivers of expedited reporting	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 safety-related recommendations	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 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. Information Users

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. Improved Information Technology

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. Duplication 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. Small Businesses

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. Less Frequent Collection

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

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

## 8. Federal Register Notice/Outside Consultation

In accordance with 5 CFR 1320.8(d), FDA published a notice in the FEDERAL REGISTER of November 20, 2001 (66 FR 58151, Tab B) providing for a 60-day comment period on the information collection. FDA received a number of comments on the draft guidance, however, only one letter of comment included a comment regarding the information collection provisions. The comment stated that the Hours per Response were underestimated for the SOPS and Data Analysis Plan (statistical approach) listed in Table 1 for the Estimated Annual Reporting Burden. The comment requested an increase to 12 hours for these burdens from the previous estimate of 4 hours for the SOPs, and 8 hours for the Data Analysis Plan.

FDA also published a notice in the FEDERAL REGISTER of December 30, 2005 (70 FR 77403) provided a 30-day public comment period on the information collection. Quintiles submitted to OMB a number of comments in one letter which have been reviewed. The specific responses on two issues related to the information collection are (numbered as in Quintiles letter of January 30, 2006):

10. Provision of Data: This comment relates to the relative timeliness of the data summarized and reported to the DMC. The amount of time available for data cleaning prior to preparing a DMC report is certainly limited in an interim analysis process and, as such, there must be a balance reached on a case-by-case basis, as a function of the trial design, conduct, operational aspects, etc.

12. Data Provision to the DMC: The technology solutions do continue to evolve. This guidance document was intended to discuss establishment and operation of DMCs, but was not intended to address the impact of new technologies on various processes. The DMC members will come to an agreement with the sponsor on the format of the information provided to them, as a part of the development of a DMC charter (Section 4.3).

Since both of these comments regard topics that are not addressed in the guidance they are outside the scope for information collections purposes.

In revising the draft guidance, FDA is adding the applicable regulations throughout the guidance including the regulations associated with these two burden estimates. The burden associated with the submission of SOPS and the statistical approach in Table 1 is covered under §§ 312.23 and 812.150(b)(10) and approved under OMB Package Number 0910-0014 and 0910-0078. Therefore, these categories were removed from table 1 and no change in the burden estimates is necessary.

## 9. Payment/Gift to Respondents

No payment or gift was provided to respondents.

## 10. Confidentiality

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. Sensitive Questions

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

12. Burden Estimate (Total Hours and Wages)

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

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 of expedited reporting	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 safety-related recommendations	37	1	37	.5	18.5
Total					758.75

Reporting 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 currently 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	\$42.00	\$787.50
Reporting	740	\$69.00	\$51,060.00
Recordkeeping	740	\$69.00	\$51,060.00
Recordkeeping	296	\$42.00	\$12,432.00
Total			\$115,339.50

The annual cost to the respondents is estimated at \$115,339.50. The cost is based on a regulatory affairs specialist (\$38/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 (\$64/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. Capital Cost (Maintenance of Capital Costs)

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

14. Cost to the Federal Government

The estimated annualized cost to the Federal Government is \$23,976. 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 (\$54/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	\$54.00	\$23,976

15. Program or Burden Changes

Changes in burden are not applicable as this is the first submission for the guidance document.

16. Publication and Tabulation Dates

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

17. Display of OMB Approval Date

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 Submission"

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