SUPPORTING STATEMENT

Guidance for Industry on Special Protocol Assessment

Docket Number 2004N-0103

0910-0470

A. Justification

1. Circumstances of Information Collection

This information collection approval request is for a Food and Drug Administration (FDA) guidance for industry entitled "Special Protocol Assessment," which describes agency procedures to evaluate issues related to the adequacy (e.g., design, conduct, analysis) of certain proposed studies. The guidance describes procedures for sponsors to request special protocol assessment and for the agency to act on such requests. The guidance provides information on how the agency will interpret and apply provisions of the Food and Drug Administration Modernization Act of 1987 and the specific Prescription Drug User Fee Act of 1992 (PDUFA) goals for special protocol assessment associated with the development and review of PDUFA products.

The guidance describes two collections of information: (1) The submission of a notice of intent to request special protocol assessment of a carcinogenicity protocol, and (2) the submission of a request for special protocol assessment.

A. Notification for a Carcinogenicity Protocol

As described in the guidance, a sponsor interested in agency assessment of a carcinogenicity protocol should notify the appropriate division in FDA's Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER) of an intent to request special protocol assessment at least 30 days prior to submitting the request. With such notification, the sponsor should submit relevant background information so that the agency may review reference material related to carcinogenicity protocol design prior to receiving the carcinogenicity protocol.

B. Request for Special Protocol Assessment

In the guidance, CDER and CBER ask that a request for special protocol assessment be submitted as an amendment to the investigational new drug application (IND) for the underlying product and that it be submitted to the agency in triplicate with Form FDA 1571 attached. The agency also suggests that the sponsor submit the cover letter to a request for special protocol assessment via facsimile to the appropriate division in CDER or CBER. Agency regulations (? 312.23(d)) state that information provided to the agency as part of an IND is to be submitted in triplicate and with the appropriate cover form, Form FDA 1571. An IND is submitted to FDA under existing regulations in part 312 (21 CFR part 312),

which specifies the information that manufacturers must submit so that FDA may properly evaluate the safety and effectiveness of investigational drugs and biological products. The information collection requirements resulting from the preparation and submission of an IND under part 312 have been estimated by FDA and the reporting and recordkeeping burden has been approved by OMB until January 31, 2006, under OMB Control Number 0910-0014.

FDA suggests that the cover letter to the request for special protocol assessment be submitted via facsimile to the appropriate division in CDER or CBER to enable agency staff to prepare for the arrival of the protocol for assessment. The agency recommends that a request for special protocol assessment be submitted as an amendment to an IND for two reasons: (1) To ensure that each request is kept in the administrative file with the entire IND, and (2) to ensure that pertinent information about the request is entered into the appropriate tracking databases. Use of the information in the agency's tracking databases enables the appropriate agency official to monitor progress on the evaluation of the protocol and to ensure that appropriate steps will be taken in a timely manner.

CDER and CBER have determined and the guidance recommends

that the following information should be submitted to the appropriate Center with each request for special protocol assessment so that the Center may quickly and efficiently respond to the request:

? Questions to the agency concerning specific issues regarding the protocol; and

? All data, assumptions, and information needed to permit an adequate evaluation of the protocol, including: (1) The role of the study in the overall development of the drug; (2) information supporting the proposed trial, including power calculations, the choice of study endpoints, and other critical design features; (3) regulatory outcomes that could be supported by the results of the study; (4) final labeling that could be supported by the results of the study; and (5) for a stability protocol, product characterization and relevant manufacturing data.

2. Purpose and Use of Information

As explained above, the procedures and policies described in the guidance document are designed to implement section 505(b)(4)(B) of the act and the PDUFA goals for special protocol assessment and agreement.

3. Use of Improved Information Technology

The Food and Drug Administration Modernization Act of 1997 (FDAMA) and the Prescription Drug User Fee Act (PDUFA) II reauthorization mandate that the agency develop and update its information management infrastructure to allow the paperless receipt and processing of investigational new drug applications and new drug applications, as defined in PDUFA, and related submissions. In the Federal Register of December 11, 2003, FDA issued a final rule requiring the submission of labeling for human prescription drugs and biologics in electronic format. FDA has also issued several guidances describing how to make voluntary electronic submissions to the agency. In January 1999, FDA issued a guidance on general considerations for electronic submissions entitled "Providing Regulatory Submissions in Electronic Format--General Considerations." The general considerations guidance included a description of the types of electronic file formats that we are able to accept for processing, reviewing, and archiving electronic documents. In January, 1999, FDA announced the availability of a guidance entitled "Providing Regulatory Submissions in Electronic Format--NDAs," which provided information on how to submit a complete archival copy of an NDA in electronic format. In November 1999, FDA published a

guidance to assist applicants in submitting documents in electronic format for review and archive purposes as part of a BLA, product license application (PLA), or establishment license application (ELA). Most recently, FDA published a guidance for ANDAs, “Providing Regulatory Submission in Electronic Format–-ANDAs” (June 27, 2002), and “Providing Regulatory Submission in Electronic Format–- Annual Reports for NDAs and ANDAs" (August 2003).

4. Efforts to Identify Duplication

The information collection requested under the guidance does not duplicate any other information collection.

5. Involvement of Small Entities

Although new drug development is typically an activity completed by large multinational drug firms, the information collection requested under the guidance applies to small as well as large companies. Under the Regulatory Flexibility Act, FDA regularly analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements.

6. Consequences If Information Collected Less Frequently

As explained above, the guidance sets forth procedures adopted by CDER and CBER to evaluate issues related to the adequacy (e.g., design, conduct, analysis) of certain proposed studies. The guidance describes procedures for sponsors to request special protocol assessment and for the agency to act on such requests.

7. Consistency with the Guidelines in 5 CFR 1320.5(d)(2)

There is no inconsistency with the guidelines.

8. Consultation Outside the Agency

In the Federal Register of March 22, 2004, (69 FR 13304), the agency requested comments on the proposed collection of information. No comments were received.

9. Remuneration of Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under this guidance.

10. Assurance of Confidentiality

Confidentiality of the information submitted under this

guidance is protected under 21 CFR 312.130 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the act.

11. Questions of a Sensitive Nature

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden

The table below provides an estimate of the annual reporting burden for requests for special protocol assessment. The procedures for requesting special protocol assessment that are set forth in the guidance document have not been previously described by the agency, although the PDUFA goals and the requirements of section 505(b)(4)(B) of the act have been in effect since October and November 1998, respectively.

Notification for a Carcinogenicity Protocol. Based on data collected from the review divisions and offices within CDER and CBER, including the number of notifications for carcinogenicity protocols and the number of carcinogenicity protocols submitted in fiscal year (FY) 2003, CDER estimates that it will receive approximately 40 notifications of an intent to request special protocol assessment of a

carcinogenicity protocol per year from approximately 20 sponsors. CBER anticipates 1 notification. The hours per response, which is the estimated number of hours that a sponsor would spend preparing the notification and background information to be submitted in accordance with the guidance, is estimated to be approximately 8 hours.

Requests for Special Protocol Assessment. Based on data collected from the review divisions and offices within CDER and CBER, including the number of requests for special protocol assessment submitted in FY 2003, CDER estimates that it will receive approximately 273 requests for special protocol assessment per year from approximately 102 sponsors. CBER estimates that it will receive approximately 20 requests from approximately 12 sponsors. The hours per response is the estimated number of hours that a respondent would spend preparing the information to be submitted with a request for special protocol assessment, including the time it takes to gather and copy questions to be posed to the agency regarding the protocol and data, assumptions, and information needed to permit an adequate evaluation of the protocol. Based on the agency's experience with these submissions, FDA estimates approximately 15 hours on average would be needed per response. Overall, FDA estimates that respondents will spend

4,523 hours per year to participate in the programs described in the guidance document.

FDA estimates the burden of this collection as follows:

Table 1. Estimated Annual Reporting Burden[1]

	No. of Respondents	Number of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
Notification for Carcinogenicity Protocols	21	1.78	41	8	328
Requests for Special Protocol Assessment	114	2.57	293	15	4,395
Total					4,723

[1]There are no capital costs or operating and maintenance costs associated with this collection.

13. Estimates of Annualized Cost Burden to Respondents

FDA's Economics Staff estimates an average industry wage rate of $50.00 per hour for preparing and submitting the information requested under the guidance. This figure is an average of the following wage rates (based on the percentage of time required for each type of employee): Upper management at $70.00 per hour; middle management at $35.00 per hour; and clerical assistance at $23.00 per hour. Using the averaged wage rate of $50.00 per hour, and multiplied times the total hour burden estimated above, the total cost burden to respondents is $236,150.00.

14. Estimates of Annualized Cost Burden to the Government

FDA estimates that there will be no additional costs associated with the receipt/review by FDA of the information submitted under the guidance.

15. Changes In Burden

The change in burden is the result of an increase in data submissions over the past 3 years.

16. Time Schedule, Publication, and Analysis Plans

There are no publications.

17. Displaying of OMB Expiration Date

The agency is not seeking to display the expiration date for
OMB approval of the information collection.

18. Exception to the Certification Statement - Item 19

There are no exceptions to the certification statement identified in Item 19, "Certification for Paperwork Reduction Act
Submission," of OMB Form 83-I.

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