

SUPPORTING STATEMENT

Guidance for Industry on Formal Dispute Resolution; Appeals Above the Division Level

0910-0430

A. Justification

1. Circumstances of Information Collection

This information collection approval request is for a Food and Drug Administration (FDA) guidance on the process for formally resolving scientific and procedural disputes in the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) that cannot be resolved at the division level. The guidance describes procedures for formally appealing such disputes to the office or center level and for submitting information to assist center officials in resolving the issue(s) presented. The guidance provides information on how the agency will interpret and apply provisions of the existing regulations regarding internal agency review of decisions (Sec. 10.75) and dispute resolution during the IND process (Sec. 312.48) and the NDA/ANDA process (Sec. 314.103). In addition, the guidance provides information on how the agency will interpret and apply the specific PDUFA goals for major dispute resolution associated with the development and review of PDUFA products.

Existing regulations, which appear primarily in parts 10, 312, and 314 (21 CFR parts 10, 312, and 314), establish procedures for the resolution of scientific and procedural disputes between interested persons and the agency, CDER, and CBER. All agency decisions on such matters are based on information in the administrative file (Sec. 10.75(d)). In general, the information in an administrative file is collected under existing regulations in parts 312 (OMB Control No. 0910-0001), 314 (OMB Control No. 0910-0014), and part 601 (21 CFR

part 601) (OMB Control No. 0910-0315), which specify the information that manufacturers must submit so that FDA may properly evaluate the safety and effectiveness of drugs and biological products. This information is usually submitted as part of an IND, NDA, or biologics license application (BLA), or as a supplement to an approved application. While FDA already possesses in the administrative file the information that would form the basis of a decision on a matter in dispute resolution, the submission of particular information regarding the request itself and the data and information relied on by the requestor in the appeal would facilitate timely resolution of the dispute. The guidance describes the following collection of information not expressly specified under existing regulations: The submission of the request for dispute resolution as an amendment to the application for the underlying product, including the submission of supporting information with the request for dispute resolution.

Agency regulations (Secs. 312.23(11)(d), 314.50, 314.94, and 601.2) state that information provided to the agency as part of an IND, NDA, ANDA, or BLA is to be submitted in triplicate and with an appropriate cover form. Form FDA 1571 must accompany submissions under IND's and Form FDA 356h must accompany submissions under NDA's, ANDA's, and BLA's. Both forms have valid OMB control numbers as follows: FDA Form 1571, OMB Control No. 0910-0014, expires December 31, 1999; and FDA Form 356h, OMB Control No. 0910-0338, expires April 30, 2000.

In the guidance document, CDER and CBER ask that a request for formal dispute resolution be submitted as an amendment to the application for the underlying product and that it be submitted to the agency in triplicate with the appropriate form attached, either Form FDA 1571 or Form FDA 356h. The agency recommends that

a request be submitted as an amendment in this manner for two reasons: To ensure that each request is kept in the administrative file with the entire underlying application and 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 resolution of the dispute 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 dispute resolution so that the Center may quickly and efficiently respond to the request: (1) A brief but comprehensive statement of each issue to be resolved, including a description of the issue, the nature of the issue (i.e., scientific, procedural, or both), possible solutions based on information in the administrative file, whether informal dispute resolution was sought prior to the formal appeal, whether advisory committee review is sought, and the expected outcome; (2) a statement identifying the review division/office that issued the original decision on the matter and, if applicable, the last agency official that attempted to formally resolve the matter; (3) a list of documents in the administrative file, or additional copies of such documents, that are deemed necessary for resolution of the issue(s); and (4) a statement that the previous supervisory level has already had the opportunity to review all of the material relied on for dispute resolution. The information that the agency suggests submitting with a formal request for dispute resolution consists of: (1) Statements describing the issue from the perspective of the person with a dispute, (2) brief statements describing the

history of the matter, and (3) the documents previously submitted to FDA under an OMB approved collection of information.

2. Purpose and Use of Information

The guidance is intended to provide guidance for industry on procedures that will be adopted by CDER and CBER for resolving scientific and procedural disputes that cannot be resolved at the division level. As explained above, CDER and CBER have determined that the information specified in the guidance should be submitted to the appropriate center with each request for dispute resolution so that the Center may quickly and efficiently respond to the request.

3. Use of Improved Information Technology

In the mid-1980's, FDA began working with pharmaceutical sponsors to develop Computer-Assisted New Drug Applications (CANDA). CANDAs were designed to provide information (text, data, image) electronically to facilitate the review of applications. These efforts yielded valuable information but were limited because for each new drug review division sponsors tended to develop different hardware and software approaches. A reviewer might be confronted with an array of hardware, software, and review tools to conduct a review that differed between sponsors and applications. Also, CANDAs were never approved as a substitute for the archival copy, so firms were still required to submit copies.

One solution to limitations of CANDAs was an approach whereby staff responsible for a particular review discipline (eg, chemistry, clinical) worked directly with pharmaceutical sponsors to develop a consistent approach that would be applicable to all sponsors and to all review divisions. Focus on this approach has

evolved into the Electronic Regulatory Submission and Review (ERSR) Program. This new initiative is intended to ensure both the electronic availability of information and the means to manipulate this information electronically to yield a review.

ERSR has been made possible by other developments. The harmonization of FDA Form 356h has ensured that NDAs, ANDAs, and Biological License Applications would contain comparable information in the same sections of the submission. The promulgation of the "Electronic Records; Electronic Signatures" final rule allowed FDA to accept electronic submissions without an accompanying paper archival copy because electronic records are equivalent to paper records and electronic signatures are equivalent to hand-written signatures provided the requirements of 21 CFR Part 11 are met and the document has been identified in the agency's public docket as being acceptable for filing. The Guidance for Industry on "Archiving Submissions in Electronic Format - NDAs" provides for the receipt and archival of electronic report forms and tabulations. Another guidance for industry on "Providing Regulatory Submissions in Electronic Format - NDAs" issued in January 1999.

ERSR is made up of a variety of projects that are in different stages of development and implementation. These projects are categorized into 3 areas: First, "Electronic Submissions" includes standards-related projects to define the format and content of regulatory submissions; written guidance for industry to follow in preparing electronic submissions; an Electronic Document Room project to accommodate the receipt, archive, and storage of electronic transmissions; an Electronic Gateway project to provide an agency-level central point for receipt of secure electronic transmissions and routing to the Centers; and scientific databases that include structured

databases, reference guides, and analytical tools used by reviewers. Second, "Corporate Databases, Documentbases and Applications" includes projects under the Electronic Document Management System and the Management Information System. Third, other electronic initiatives including technical infrastructure, technical support, and training.

ERSR will impact the underlying business processes related to regulatory submissions and reviews. Document rooms will handle electronic media rather than paper copies. Reviewers will review submissions online and generate their review documents online. Reviewers will conduct data analysis using structured databases, which combine data extracted from the submission under review as well as historical data from earlier submissions. Industry sponsors and manufacturers will experience reduced paper costs and manpower to compile paper submissions and better access to application status information through electronic mail.

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, CDER and CBER have determined that the information specified in the guidance should be submitted to the appropriate center with each request for dispute resolution so that the Center may quickly and efficiently respond to the request.

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

There is no inconsistency with the guidelines.

8. Consultation Outside the Agency

A draft guidance was published with opportunity for public comment in the Federal Register of March 19, 1999 (64 FR 13587). One comment was received. The comment stated that FDA's estimate is a relatively accurate accounting of time used in administrative preparation of information for routine meetings. The comment stated that FDA underestimated the time required for creative writing and editing tasks associated with preparation of paperwork prior to a formal meeting where many issues or complicated topics will be discussed.

The agency's estimates are based in part on the expectation that respondents will have already compiled for submission to the agency most of the data and information that is described in the guidance document. The agency anticipates that respondents will have submitted the information as part of the underlying product application. Therefore, the bulk of the paperwork burden is related to administrative tasks, i.e., gathering and copying brief statements about the product and describing details of the anticipated meeting.

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 314.430 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

Based on FDA's experience with dispute resolution, the agency expects that most persons seeking formal dispute resolution will have gathered the materials listed previously when identifying the existence of a dispute with the agency. Consequently, FDA anticipates that the collection of information attributed solely to the guidance will be minimal. Provided below is an estimate of the annual reporting burden for requests for dispute resolution. In fiscal year (FY) 1998, 39 sponsors and applicants (respondents) submitted requests for formal dispute resolution to CDER and 12 respondents submitted requests for formal dispute resolution to CBER. Although the procedures for requesting formal dispute resolution that are set forth in the guidance document were not in place in FY 1998, FDA estimates that the number of respondents who would submit requests for dispute resolution under the guidance would remain the same. The total annual responses are the total number of requests submitted to CDER and CBER in 1 year, including requests for dispute resolution that a single respondent submits more than one time. In FY 1998, CDER received approximately 49 requests and CBER received approximately 15 requests. The agency estimates that the total annual responses will remain the same, averaging to 1.26 responses per respondent. 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 formal dispute resolution in accordance with this guidance, including the time it takes to gather and copy brief statements describing the issue from the perspective of the person with the dispute, brief statements describing the history of the matter, and supporting information that has already been submitted to the agency. Based on experience, FDA estimates that approximately 8 hours on average would be needed per response. Therefore, FDA estimates that 512 hours will be spent per year by respondents requesting formal dispute resolution under the guidance.

Estimated Annual Reporting Burden

Requests for Formal Dispute Resolution	Number of Respondents	Number of Responses Per Respondent	Total Annual Responses	Hours Per Response	Total Hours
CDER	39	1.26	49	8	392
CBER	12	1.25	15	8	120
Total					512

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 \$25,600.00.

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.

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15. **Publication of Information Collection Results**

FDA does not intend to publish tabulated results of the information collection requirements that would be imposed by these regulations.

16. **Time Schedule, Publication and Analysis Plans**

There are no publications.

17. **Display of OMB Approval**

The required reporting forms accurately reflect the OMB approval number

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.

