Orphan Drug Products
OMB No. 0910-0167
SUPPORTING STATEMENT

1. Circumstances Necessitating Information Collection

This is a request for OMB approval of the information collection requirements in the Orphan Drug Regulations, 21 CFR Part 316 (Attachment A). These provisions implement sections 525 through 528 (Attachment B) of the Orphan Drug Act Amendments to the Federal Food, Drug, and Cosmetic Act (the act). These regulations specify the procedures for sponsors of orphan drugs to use in obtaining the incentives provided for in the Act and set forth the procedures that FDA will use in administering the Act.

Section 525 of the Act (21 USC 360aa) requires the Agency to provide written recommendations on studies required for approval of a marketing application for a drug for a rare disease or condition. Section 526 of the Act (21 USC 360bb) provides for designation of drugs as orphan drugs when certain conditions are met. Section 527 of the Act (21 USC 360cc) provides conditions under which a sponsor of an approved orphan drug enjoys exclusive FDA marketing approval for that drug for the orphan indication for a period of seven years.

Section 528 of the Act (21 USC 360dd) is to encourage sponsors to make investigational orphan drugs available for treatment of persons in need on an open protocol basis before the drug has been approved for general marketing. Open protocols may permit patients who are not part of the formal clinical investigation to obtain treatment where adequate supplies exist and no alternative effective therapy is available.

These regulations describe the information to be submitted by sponsors to request eligibility for the incentives by implementing a program as outlined in the Orphan Drug Act. The following provisions identify the information collections contained in the regulation.

21 CFR 316.10 - Reporting
Specifies the procedures for a sponsor to follow when requesting a written recommendation from FDA concerning the clinical and non-clinical investigations necessary for the approval of a marketing application.

21 CFR 316.12 - Reporting
Specifies that prior to receiving a written recommendation from FDA, a sponsor may be required to submit for Agency review, the results of non-clinical studies or completed early clinical studies.

21- CFR 316.14- Reporting
Specifies the detailed procedures to be followed by a sponsor when FDA refuses to provide a written recommendation.

21 CFR 316.20 - Reporting
Specifies the content and format a sponsor must submit a request for orphan-drug designation.

21 CFR 316.21 - Reporting
Specifies the content and format a sponsor must follow when seeking to obtain orphan-drug designation of a drug for a disease or condition affecting less than 200,000 persons in the United States.

21 CFR 316.22 - Reporting
Requires that upon the nomination of a permanent resident-agent by a foreign sponsor seeking orphan-drug designation, the name of the agent shall be submitted to the FDA Office of Orphan Products.

21 CFR 316.26 - Reporting
Specifies the requirements when a sponsor wishes to apply for an amendment to an orphan-drug designation prior to approval of the marketing application.

21 CFR 316.27 Reporting
Specifies information to be submitted to FDA during a change in ownership of orphan-drug designation.

21 CFR 316.30 - Reporting
Requires that within 14 months after a drug is designated as an orphan-drug (and, annually, thereafter) the sponsor shall submit a brief progress report to FDA until marketing approval.

21 CFR 316.36 - Reporting
Specifies that a sponsor seeking to retain orphan-drug exclusivity, after an FDA determination, cannot assure the availability of sufficient quantities of an orphan-drug to meet the needs of affected persons.

2. <u>How, By Whom, Purpose of Collection</u>

FDA uses the requested information to make the determination that the drug is for a legitimately rare disorder and issue an orphan-drug designation. Secondly, the information describes the sponsor's plan for clinical and preclinical studies.

Review of the sponsor’s protocol will allow the Agency to provide guidance to the sponsor that may allow him to eliminate plans for costly and unnecessary studies. FDA may also suggest adding studies or making other changes that will result in a plan that conforms to FDA requirements. Data obtained from well-designed studies will be, therefore, useful in demonstrating safety and effectiveness of the drug for the rare disease or condition. Failure to collect this information will seriously impair the FDA’s ability to guide the sponsor needing such recommendations, and may result in the sponsor dedicating substantial resources and losing valuable time in doing studies that are not necessary or are irrelevant to obtaining FDA market approval.

3. Considerations Given to Information Technology

Improved technology for filing of pre-clinical and clinical information is currently being considered by operating drug and biological review Centers in FDA. Changes made in such technologies will be adopted when appropriate within the procedures of the FDA drug review and orphan products development programs.

4. Identification of Information

Since the collection of data is specifically for application for incentives under the Orphan Drug Act, there is little possibility that other agencies are collecting similar information.

5. Small Business Considerations

The provisions of the Orphan Drug Act and the provisions contained in the regulations are favorable to small business interests. The orphan-drug designation provision entitles the sponsor to Federal income tax credits for clinical studies, and eligibility for grants to fund studies of orphan products. The Orphan Drug Exclusivity Provision provides protection from competition by other companies that is administered by FDA. A larger company cannot get around this protection by simply marketing the same product and forcing the small manufacturer into a costly court battle, as with a patent. The FDA by law must insure that a competitive product does not enter the market by withholding approval of a subsequent new drug application or biological license application.

6. Consequences of Less Frequent Collection

The frequency of the collection of the data is entirely controlled by the sponsor requesting eligibility for one of the incentives of the Orphan Drug Act.

7. Special Circumstances

The method of collection is consistent with the guidelines of 5 CFR 1320.6.

8. Outside Consultation

In accordance with 5 CFR 1320.8(d), a 60-day notice for public comment on the information collection provisions was published in the **Federal Register** of October 30, 2006 (71 FR 63325) to which no comments were received.

Orphan Product Development staff regularly attend public meetings of industry organizations, clinical investigators, patient groups, and other similar events. No comments or suggestions relative to the requirements have been received through this source. In addition, FDA maintains an active Web Site and a toll-free phone line for its orphan product program where concerns about the requirements or their modification can be readily submitted and has received none.

9. Explanation of Any Payment or Gift to Respondents

There are no payments or gifts to respondents

10. Assurances of Confidentiality

The Orphan Drug Act provides that the designation of a drug as an orphan-drug should be a public event. Accordingly, 21 CFR 316.28 provides that public notice be made of all drugs designated as orphan-drugs and will include the name and address of the sponsor, the name of the drug, the rare disease or condition for which the drug was designated, and proposed indication for use. Similarly public notice is made identifying sponsors drugs and indications for use that have obtained Orphan Drug Exclusivity. 21 CFR 316.32 provides that FDA will neither publicly disclose the existence of a request for nor the substance of the request until final action is taken. Further, FDA will not publicly disclose the existence of a pending marketing application for a designated orphan-drug unless the existence of the request has been previously disclosed or acknowledged.

Determinations of public availability of data and information contained in pending and approved marketing applications will continue to be in accordance with existing provisions of 21 CFR Parts 20 and 314.430.

11. Justification for Questions of a Sensitive Nature

No questions of a sensitive nature are contained in the proposal.

12. Estimated Burden of Information Collection

Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	Annual Frequency of response	Total Annual Responses	Hours per Response	Total Hours
316.10, 316.12, & 316.14	5	1	5	130	650
316.20, 316.21, & 316.26	171	2.0	342	130	44,460
316.22	30	1	30	2	60
316.27	25	1	25	4	100
316.30	500	1	500	2	1,000
316.36	1	1	1	15	15

Total	46,285

There are no capital costs or operating and maintenance costs associated with this collection of information.

The information requested from respondents represents, for the most part, an accounting of information already in the possession of the applicant. It is estimated, based on frequency of requests over the past five years, that 171 persons or organizations per year will request orphan-drug designation and none will request formal recommendations on design of preclinical or clinical studies.

FDA estimates that the effort required to prepare the applications for consideration in both sections 525 and 526 **(**21 CFR Parts 316.10 & 316.20, respectively**)** is generally similar, and, is estimated to require an average of 98 hours of professional staff time and 32 hours of support staff time per application (98 + 32 = 130). FDA bases estimates of annual activity and burden for foreign sponsor nomination of a resident agent, change in ownership of designation, and inadequate supplies of a drug in exclusivity, on total experience with such requests since 1983.

For 316.10, 316.12, and 316.14, five requests for recommendations are anticipated.

For 316.20, 316.21, and 316.22, 342 responses related to Designation as Orphan Drug Annually x 130 hours per response (98 hours professional time + 32 hours support time) = 44,460 hours.

For 316.22, 30 nominations annually x 2 hours per response (1 hour professional time + 1 hour support time) = 60 hours.

For 316.27, 25 changes annually x 4 hours per response (2 hours professional time + 2 hours support time.) = 100 hours.

For 316.30, 500 reports annually x 2 hours per response (1 hour professional time + 1 hour support time) = 1,000 hours.

For 316.36, one action every five years or .6 responses annually x 15 hours per response (10 hours professional time + 5 hours support time) = 9 hours.

Cost to Respondents			
Activity	Number of Hours	Cost per Hour	Total Cost
Request for Designation	33,345 11,115	$75 $15	2,500,875 166,725
Foreign Sponsor	30	$75	2,250

Nominate	30	$15	450
Change in Ownership	25 25	$75 $15	1,875 375
Annual Report	500 500	$75 $15	37,500 7,500
Inadequate Supplies	6 3	$75 $15	450 45
		Total	$2,718,045

For purposes of calculating costs to respondents, we utilized an estimated average for professional response time at $75.00 per hour and per hour costs for support hour at $15.00. These estimates based on discussions with prior respondents related to the salary levels and types of personnel assigned to obtain and present the information required. The hourly input per requirement utilizes the information in the preceding table.

13. Other Costs to Respondents

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

14. Costs to the Federal Government

FDA estimates that the equivalent of five full time positions ranging from GS-5 clerical personnel to GS-15 medical officers ($84,000 for personnel costs and benefits and $6,000 of operating funds per year at a total cost of $450,000) will be required to fully implement the collection of information, response to applicants, guidance and recommendations to sponsors required by the applicable law and regulations. The estimates are based on knowledge of resources used by the FDA Office of Orphan Products Development in implementing the Orphan Drug Act over the last 18 years. Since the number of applications is expected to continue at the same annual rate, past FDA experience will be a good predictor of future resource needs.

15. Reason for Change

Based on the increased number of requests for orphan product designations over the past three years, FDA increased the number of respondents for this collection of information resulting in a total burden increase of 8,942 hours.

16. Statistical Reporting

The objectives of the collection are not for publication of statistical material and do not employ statistical methods.

17. Display of OMB Approval Date

FDA is not seeking approval to exempt display of the expiration date for OMB approval.

18. Exceptions to "Certification for Paperwork Reduction Act Submissions"

n/a