Orphan Products Development; Food and Drug Administration Orphan Drug Designation

OMB No. 0910-0167

SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

This is a request for OMB approval of the information collection requirements in the Orphan Drug Regulations, 21 CFR Part 316. These provisions implement sections 525 through 528 of the Orphan Drug Act Amendments to the Food, Drug, and Cosmetic 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.

We are consolidating into this request for approval 0910-0787, "Guidance for Industry, Researchers, Patient Groups, and Food and Drug Administration Staff on Meetings With the Office of Orphan Products Development". The guidance describes three collections of information: (1) The submission of a meeting request (for informal and formal meeting), (2) the submission of a meeting package (for formal meetings), and (3) the submission of draft meeting minutes (for formal and certain informal meetings).

The collection of information described in this guidance is intended to provide background information in support of consistent procedures to promote well-managed meetings between OOPD and stakeholders. In some cases, these meetings may represent a critical point in the orphan product development process and may even

have an impact on the eventual availability of products for patients with rare diseases and conditions. It is therefore important that these meetings be scheduled within a reasonable time, conducted effectively, and documented where appropriate.

2. Purpose and Use of the Information Collection

Orphan-drug designation provides financial incentives for the development of a drug for the diagnosis, prevention, or treatment of a rare disease or condition.

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

The guidance regarding meetings provides recommendations to industry, researchers, patient groups, and other stakeholders (collectively referred to as "stakeholders") interested in requesting a meeting with FDA's Office of Orphan Products Development (OOPD) on issues related to orphan drug designation requests, humanitarian use device (HUD) designation requests, rare pediatric disease designation requests, funding opportunities through the Orphan Products Grants Program and the Pediatric Device Consortia Grants Program, and orphan product patient-related topics of concern. This guidance document is intended to assist these groups with requesting, preparing, scheduling, conducting, and documenting meetings with OOPD and will provide for more productive meetings with stakeholders.

3. Use of Improved Information Technology and Burden Reduction

Improved technology for submission of orphan drug designation and meeting requests is currently being developed by the Office of Orphan Products Development in FDA. Changes made in such technologies will be adopted when appropriate within the procedures of FDA orphan products development programs.

4. Efforts to Identify Duplication and Use of Similar 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. Impact on Small Businesses or Other Small Entities

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. The FDA must by law insure that a competitive product

does not enter the market by withholding approval of a subsequent new drug application or biological license.

6. Consequences of Collecting the Information Less Frequently

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. There are no legal obstacles to reduce the burden.

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

The method of collection is consistent with the guidelines of 5 CFR 1320.6. There are no special circumstances for this collection of information.

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 60-day notice for public comment on the information collection provisions was published in the Federal Register of October 2, 2020 (85 FR 62306) to which no comments were received.

9. Explanation of Any Payment or Gift to Respondents

There are no payments or gifts provided to respondents.

10. Assurance of Confidentiality Provided to Respondents

In preparing this Supporting Statement, we consulted our Privacy Office to ensure appropriate identification and handling of information collected.

This ICR collects personally identifiable information (PII) or other data of a personal nature. PII is collected in the context of the subject individuals' professional capacity and the FDA-related work they perform for their employer (e.g., point of contact at a regulated entity). The PII submitted via Form FDA 4035(The Food and Drug Administration Orphan Drug Designation Request Form) and Form FDA 3671 (The Common European Medicines Agency (EMA)/Food and Drug Administration (FDA) Application Form for Orphan Medicinal Product Designation) is name, business email address, business telephone number, and business fax telephone number.

Sponsors seeking orphan designation of the same drug for the same disease or condition from both FDA and EMA may use this common application form for regulatory filing purposes. The Food and Drug Administration Orphan Drug Designation Request Form 4035 is intended to benefit sponsors who desire to seek orphan designation of drugs intended for rare diseases or conditions from only FDA. Both forms are intended to complement, not supersede, the relevant regulatory frameworks currently in effect. When using the common application form, the sponsor must comply with all applicable regulatory requirements in each jurisdiction in which

designation is sought.

Under the Freedom of Information Act (FOIA) (5 U.S.C. 552), the public has broad access to government documents. However, FOIA provides certain exemptions from mandatory public disclosure of government records (5 U.S.C. 552(b)(1-9)). FDA will make the fullest possible disclosure of records to the public, consistent with the rights of individuals to privacy, the property rights of persons in trade and confidential commercial or financial information.

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 the 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 Sensitive Questions

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

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden and Cost

21 CFR Section; Activity	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Content and format of a request for designation; request for verification of status; amendment to designation	534	1.25	668	135	90,180
§§ 316.20, 316.21, 316.26 (Form FDA 4035)	534	1.25	668	32	21,376
§ 316.22; Notifications of changes in agents	132	1	132	2	264
§ 316.24(a); Deficiency letters and granting orphan-drug designation	20	1	20	2	40
§ 316.27; Submissions to change ownership of orphan-drug designation	104	1	104	5	520
§ 316.30; Annual reports	744	1	744	3	2,232
§ 316.36; Assurance of the availability of sufficient quantities of the orphan drug; holder's consent for the approval of other marketing applications for the same drug	1	3	3	15	45
Guidance Recommendations: Meeting requests to OOPD and related submission packages	2,508	1	2,508	3.595	9,016
Total					123,673

[1] 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 four years, that 534 persons or organizations per year will request orphan drug designation and it is anticipated

there will be no requests for a formal recommendation on design or preclinical or clinical studies.

FDA estimates that the effort required for consideration in both sections 525 and 526 (21 CFR Parts 316.10 & 316.20, respectively) is an average of 110 hours of professional time and 25 hours of support staff time per application (110 + 25 = 135 hours). Estimates of annual activity and burden for foreign sponsor nominations of a resident agent, change in ownership of designations, and inadequate supplies of a drug in exclusivity, are based on total experience by FDA with such requests since 1983.

For 316.10, 316.12, and 316.14, no requests for recommendations are anticipated.

12b. Annualized Cost Burden Estimate

Activity	No. of Hours	Cost per Hour	Total Cost
Request for Orphan	73,480		$6,245,800
Designation	16,700	Professional $85	417,500
		Support Staff	
	18,036		1,533,060
Form FDA 4035	3,340		83,500
Change in	132	Professional $85	11,220
Ownership	132	Support Staff 25	3,300
Foreign Sponsor	208	Professional $85	17,680
Nominate	312	Support Staff 25	4,725
Annual Report	744	Professional $85	63,240
	1,488	Support Staff 25	37,200
Inadequate Supplies	30	Professional $85	2,250
	15	Support Staff 25	375
Deficiency Letters	40	Professional $85	3,400
		Support Staff 25	
Meetings	7,508	Professional $85	638,180
	1,508	Support Staff 25	37,700
			$9,099,130

For purposes of calculating costs to respondents, we utilized an estimated average for professional response time at $85.00 per hour and $25.00 per hour for support hour. The hourly input per requirement utilizes the information in the preceding table. The two totals in the "No. of Hours" column is separated based on professional and support staff costs and when added together represents the total burden hours for that activity. For instance, for "Requests for Orphan Designation," 73,480 + 16,700 = 90,180 as seen in item 12a of this document, first line of the table. Those separated totals are multiplied by either the professional or support staff cost. For instance, "Requests for Orphan Designation," 73,480 x $85 = $6,245,800; 16,700 multiplied by $25 = 417,500.

13. Estimates of Other Total Annual Costs to Respondents and/or Record Keepers/Capital Costs

There are no capital, start-up, or operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

FDA estimates that the equivalent of eleven full time positions ranging from GS-9 clerical personnel to GS-15 medical officers ($2,750,000 for personnel costs and benefits) will be required to implement the collection of information, response to applicants, guidance and recommendation 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 30 years. Since the number of applicants is expected to continue to increase, past FDA experience will be a good predictor of future resources.

15. Explanation for Program Changes or Adjustments

The total number of requests for orphan designation have increased as a result of increased interest by the public and pharmaceutical industry in developing products for people with rare diseases and conditions. The burden was adjusted to reflect this increase. Since there is an increase of applications, sponsors who request a designation from only the FDA have the option of submitting the FDA Orphan Drug Designation Request Form (FDA Form 4035). The estimated annual hourly burden, formerly estimated as 106,407 hours, has increased by 8,250 hours to a total estimated annual hourly burden of 114,657 hours.

We are consolidating into this request for approval 0910-0787, "Guidance for Industry, Researchers, Patient Groups, and Food and Drug Administration Staff on Meetings With the Office of Orphan Products Development" which represents an additional increase in total burden hours of 9,016 hours.

Therefore, the increase in total burden hours is 17,266.

For the purpose of ease of entry in ROCIS the previously entered eight ICs was reduced to one IC.

16. Plans for Tabulation and Publication and Project Time Schedule

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

17. Reason(s) Display of OMB Expiration Date is Inappropriate

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

18. Exceptions to Certification for Paperwork Reduction Act Submissions

Not applicable.