



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2011-N-0015]

Agency Information Collection Activities; Proposed Collection; Comment Request; Orphan Drugs; Common European Medicines Agency/Food and Drug Administration Application Form for Orphan Drug Medicinal Product Designation

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the Federal Register concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on Common European Medicines Agency (EMA)/FDA Application Form for Orphan Drug Medicinal Product Designation (Form FDA 3671).

DATES: Submit either electronic or written comments on the collection of information by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

REGISTER]. The <https://www.regulations.gov> electronic filing system will accept comments until midnight Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2011-N-0015 for "Orphan Drugs; Common EMA/FDA Application Form for Orphan Medicinal Product Designation (Form FDA 3671)--21 CFR Part 316." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the

body of your comments and you must identify this information as "confidential."

Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public docket, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Amber Sanford, Office of Operations, Food and Drug Administration, Three White Flint North, 10A63, 11601 Landsdown St., North Bethesda, MD 20852, PRASStaff@fda.hhs.gov, 301-796-8867.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information, including each proposed extension of an existing collection of information, before

submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Orphan Drugs; Common EMA/FDA Application Form for Orphan Medicinal Product

Designation (Form FDA 3671) 21 CFR Part 316

OMB Control Number 0910-0167--Extension

Sections 525 through 528 of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360aa through 360dd) give FDA statutory authority to do the following: (1) Provide recommendations on investigations required for approval of marketing applications for orphan drugs, (2) designate eligible drugs as orphan drugs, (3) set forth conditions under which a sponsor of an approved orphan drug obtains exclusive approval, and (4) encourage sponsors to make orphan drugs available for treatment on an "open protocol" basis before the drug has been approved for general marketing. The implementing regulations for these statutory requirements have been codified under part 316 (21 CFR part 316) and specify procedures that sponsors of orphan drugs use in availing themselves of the incentives provided for orphan drugs in the

FD&C Act and sets forth procedures FDA will use in administering the FD&C Act with regard to orphan drugs.

Section 316.10 specifies the content and format of a request for written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of marketing applications. Section 316.12 provides that, before providing such recommendations, FDA may require results of studies to be submitted for review. Section 316.14 contains provisions permitting FDA to refuse to provide written recommendations under certain circumstances. Within 90 days of any refusal, a sponsor may submit additional information specified by FDA. Based on past experience, FDA estimates that there will be one respondent to §§ 316.10, 316.12, and 316.14 requiring 50 hours of human resources annually.

Section 316.20 specifies the content and format of an orphan drug application which includes requirements that an applicant document that the disease is rare (affects fewer than 200,000 persons in the United States annually) or that the sponsor of the drug has no reasonable expectation of recovering costs of research and development of the drug. Section 316.21 specifies content of a request for orphan drug designation required for verification of orphan-drug status. Section 316.26 allows an applicant to amend the applications under certain circumstances. Based on past experience, FDA estimates 496 respondents to §§ 316.20, 316.21 and 316.26, requiring 93,000 hours of human resources annually.

The Common EMA/FDA Application Form for Orphan Medicinal Product Designation (Form FDA 3671) is intended to benefit sponsors who desire to seek orphan designation of drugs intended for rare diseases or conditions from both the European Commission and FDA by reducing the burden of preparing separate applications to meet the regulatory requirements in each jurisdiction. It highlights the regulatory cooperation between the United States and the

European Union mandated by the Transatlantic Economic Council (TEC). Based on past experience, FDA estimates there will be 60 respondents using the form requiring 450 hours of human resources annually.

Section 316.22 specifies requirement of a permanent resident agent for foreign sponsors. Based on past experience, FDA estimates 70 respondents requiring 140 hours of human resources annually. Section 316.24(a) specifies a requirement that sponsors respond to deficiency letters from FDA on designation requests within 1 year of issuance of the deficiency letter, unless within that time frame, the sponsor requests an extension of time to respond. Based on past experience, FDA estimates 20 respondents requiring 40 hours of human resources annually.

Section 316.27 specifies content of a change in ownership of orphan-drug designation. Based on past experience, FDA estimates 63 respondents requiring 315 hours of human resources annually. Section 316.30 requires submission of annual reports, including progress reports on studies, a description of the investigational plan, and a discussion of changes that may affect orphan status. Based on number of orphan-drug designations, the number of respondents is estimated as 744 requiring 2,232 hours of human resources annually. Finally, § 316.36 describes information required of sponsor when there is insufficient quantity of approved orphan drug. Based on past experience, FDA estimates two respondents requiring 90 hours of human resources annually.

The information requested will provide the basis for an FDA determination that the drug is for a rare disease or condition and satisfies the requirements for obtaining orphan drug status. Secondly, the information will describe the medical and regulatory history of the drug. The

respondents to this collection of information are biotechnology firms, drug companies, and academic clinical researchers.

FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Content and format when seeking written recommendations; results of studies; amendments (316.10, 316.12 & 316.14)	1	1	1	50	50
Content and format of a request for orphan-drug designation; request for verification of orphan-drug status; amendments (316.20, 316.21 & 316.26)	496	1.25	620	150	93,000
FDA Form 3671	60	1.5	90	5	450
Notifications of changes in agents (316.22)	70	1	70	2	140
Deficiency letters and granting orphan-drug designation (316.24(a))	20	1	20	2	40
Submissions to change ownership of orphan-drug designation (316.27)	63	1	63	5	315
Annual reports (316.30)	744	1	744	3	2,232
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 (316.36)	2	3	6	15	90
Total					96,317

¹There are no capital costs or operating and maintenance costs associated with this collection of information.

FDA has experienced increases in: (1) the number of submissions to change ownership of orphan-drug designation (21 CFR 316.27), (2) the number of annual reports 21 CFR 316.30, and (3) assurances of the availability of sufficient quantities of the orphan drug and the holder's consent for the approval of other marketing applications for the same drug (21 CFR 316.36). In

contrast, however, the use of Form FDA 3671, the application form to submit for product designation to the European Medicines Agency and to the FDA Office of Orphan Products, has decreased from 6,760 to 450 total burden hours.

Dated: June 13, 2017.

Anna K. Abram,

Deputy Commissioner for Policy, Planning, Legislation, and Analysis.
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