DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-0386]

Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Orphan Drugs; Common European Medicines Agency/Food and Drug Administration Application Form for Orphan Medicinal Product Designation

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that a proposed collection of information has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995 (PRA).

DATES: Fax written comments on the collection of information by [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure that comments on the information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-7285, or emailed to oira_submission@omb.eop.gov. All comments should be identified with the OMB control number 0910-0167. Also include the FDA docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE-14526, Silver Spring, MD 20993-0002, PRAStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Orphan Drugs; Common European Medicines Agency/Food and Drug Administration Application Form for Orphan Medicinal Product Designation--21 CFR Part 316 (OMB Control Number 0910-0167)--Revision

FDA is amending the 1992 Orphan Drug Regulations, part 316 (21 CFR part 316). The 1992 regulations were issued to implement sections 525 through 528 of the Orphan Drug Act Amendments to the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 360aa through 360ee). The 1992 regulations specify the procedures for sponsors of orphan drugs to use in obtaining the incentives provided for in the FD&C Act and set forth the procedures that FDA will use in administering the FD&C Act.

The amendments are intended to clarify regulatory provisions and make minor improvements to address issues that have arisen since the issuance of the regulations in 1992. They are intended to assist sponsors who are seeking and who have obtained orphan drug designations, as well as FDA in its administration of the orphan drug program. Except with respect to the two revisions addressed further, the revisions in this rule clarify existing language and do not constitute a substantive or material modification to the approved collections of information in current part 316 (see 5 CFR 1320.5(g)). The collections of information in current part 316 have been approved by OMB in accordance with the PRA under OMB control number 0910-0167.

One revision concerns the name of the drug in an orphan-drug designation request. As provided in current § 316.20(b)(2) (Content and format of a request for orphan-drug designation), requests for orphan-drug designation must include the generic and trade name, if

any, of the drug. For some products, however, neither a generic nor trade name may be available. This can be the case for some large and complicated biological products or for any molecule for which the sponsor has not yet obtained a trade name. Under § 316.20(b)(2) as revised, requests for designation must include a chemical name or a meaningful descriptive name of the drug if neither a generic nor trade name is available. Drug names need to be meaningful to the public because the Orphan Drug Act (Public Law 97-414) requires that notice respecting designation of a drug be made available to the public (section 526(c) of the FD&C Act and § 316.28 (Publication of orphan drug designations)). Internal business codes or other similar identifiers do not suffice for publication purposes, as they do not provide meaningful notice to the public of a designation. By providing a chemical name or a meaningful descriptive name of a drug in a request for designation, if neither a generic nor trade name is available, sponsors would help ensure that the name of the product that FDA ultimately publishes upon designation is accurate and meaningful.

FDA regulations are currently silent on when sponsors must respond to a deficiency letter from FDA on an orphan-drug designation request. FDA sends such deficiency letters when a request lacks necessary information or contains inaccurate information, i.e., miscalculated prevalence estimate. This rule revises § 316.24(a) (Deficiency letters and granting orphan-drug designation) to include 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. FDA will grant all reasonable requests for an extension. In the event the sponsor fails to respond to the deficiency or request an extension of time to respond within the 1-year time frame, FDA may consider the designation request voluntarily withdrawn. This proposal is necessary to ensure that designation requests do

not become "stale" by the time they are granted, such that the basis for the initial request may no longer hold.

Sections 525 through 528 of the FD&C Act 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, specify procedures that sponsors of orphan drugs use in availing themselves of the incentives provided for orphan drugs in the FD&C Act, and set 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. 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 316.26 allows an applicant to amend the applications under certain circumstances. 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. 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.

The information requested from respondents, for the most part, is an accounting of information already in the possession of the applicant. It is estimated, based on frequency of requests over the past 3 years, that 275 persons or organizations per year will request orphan-drug designation and none will request formal recommendations on design of preclinical or clinical studies.

In the Federal Register of April 16, 2014 (79 FR 21471), FDA published a 60-day notice requesting public comment on the proposed collection of information. No comments were received.

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

Table 1.--Estimated Annual Reporting Burden[1]

21 CFR Section/FDA Form	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
316.10, 316.12, and 316.14	2	1	2	100	200
316.20, 316.21, and 316.26	225	2	450	150	67,500
Form FDA 3671	50	3	150	45	6,750
316.22	65	1	65	2	130
316.27	43	1	43	5	215
316.30	450	1	450	3	1,350
316.36	2	3	6	15	90
Total					76,235

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

Dated: October 1, 2014.

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Leslie Kux,

Assistant Commissioner for Policy.

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