

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2008N-0007]

Agency Information Collection Activities; Proposed Collection; Comment Request; Orphan Drugs; Common European Medicines Agency/Food and Drug Administration Application Form for Orphan Medicinal Product Designation (Form FDA 3671)

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 the procedures by which sponsors of orphan drugs may request eligibility for the incentives by implementing a program as outlined in the Orphan Drug Act and the joint adoption by FDA and the European Medicines Agency (EMA) of the Common EMA/FDA Application Form for Orphan Medicinal Product Designation (form FDA 3671).

DATES: Submit written or electronic comments on the collection of information by *[insert date 60 days after date of publication in the **Federal Register**]*.

ADDRESSES: Submit electronic comments on the collection of information to: <http://www.fda.gov/dockets/ecomments> or <http://www.regulations.gov>. Submit written comments on the collection of information to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Jonna Capezzuto, Office of the Chief Information Officer (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4659.

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 collection of information, FDA invites comments on these topics: (1) the clarity and ease of use of this proposed common application form; (2) whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (3) the accuracy of FDA’s estimate

of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (4) ways to enhance the quality, utility, and clarity of the information to be collected; and (5) ways to minimize the burden of the collection of information on respondents, including the use of automated collection techniques, when appropriate, and other forms of information technology.

Orphan Drugs; Common EMEA/FDA Application Form for Orphan Medicinal Product Designation (Form FDA 3671) (OMB Control Number 0910-0167)—Extension

Sections 525 and 526 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360aa and 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 act and sets forth procedures FDA will use in administering the act with regard to orphan drugs. Section 316.10 specifies the content and format of a request for written recommendations concerning the non-clinical 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 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 5 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.

The Common EMEA/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 (US) and the European Union (EU) mandated by the Transatlantic Economic Council (TEC). The TEC mandate involves the following: (1) Removal of barriers to transatlantic commerce; (2) rationalizing, reforming, and, where appropriate, reducing regulations to empower the private sector; (3) achieving more effective, systematic, and transparent regulatory cooperation to reduce costs associated with regulation to consumers and producers; (4) removing unnecessary differences between jurisdictional regulations to foster economic integration; and (5) reinforcing the existing transatlantic dialogue structures in regulatory cooperation, both by intensifying our sector-by-sector US-EU regulatory cooperation and our dialogue between OMB and the European Commission services on methodological issues.

At present, when seeking orphan designation of the same drug for the diagnosis, treatment, or prevention of the same rare disease or condition in the US and in the European Community, a sponsor must submit a designation request to FDA (in accordance with section 526 of the act) and a separate designation application to EMEA (in accordance with Regulation (EC) No. 141/2000 of December 16, 1999, and Commission Regulation (EC) No. 847/2000). In most cases, the two documents are formatted differently to meet regulatory demands, but the required core information elements are similar, with the exception of some unique regulatory requirements exclusive to each jurisdiction. Therefore, FDA and EMEA believe that a common application form will help reduce the sponsor's regulatory burden and costs to produce and submit differently-formatted request/application. In addition, a common application form may also streamline the administrative and substantive

regulatory review processes, and aid in information exchange between the agencies. In accordance with the Confidentiality Arrangements concluded on September 12, 2003, between the European Commission, EMEA, and FDA/ Department of Health and Human Services (DHHS),¹ FDA and EMEA have agreed in principle to adopt a template for the common application form as proposed in form FDA 3671.

Any sponsor seeking orphan designation of the same drug for the same disease or condition from both FDA and EMEA may use this common application form for regulatory filing purposes. A sponsor may also use this common application form when seeking designation only from FDA. This common application form is intended to complement, not to supersede, the relevant regulatory frameworks currently in effect. The sponsor must comply with all applicable regulatory requirements in each jurisdiction in which it seeks designation when using this common application form.

To use the common application form, the sponsor must provide the required information in each applicable section as instructed in the explanatory notes. Certain information elements are identified in the form as required exclusively by either FDA or EMEA regulations, and as such they must be included only in the application to that jurisdiction. Where additional explanations and/or supportive documents are necessary, the sponsor should sequentially append them at the end of the common application form in the order they appear in the form. The sponsor must also complete the declaration and signature page. For FDA, the completed common application form and required appended documents must be submitted to the Office of Orphan Products Development (HF-35), Food and Drug Administration, 5600 Fishers

¹ See “Confidentiality Arrangements Concluded Between the EU (EC and EMEA) and the US FDA/DHHS Implementation Plan for Medicinal Products for Human Use” at <http://www.fda.gov/oia/arrangements0904.html>.

Lane, Rockville, MD 20857. For EMEA, the completed documents must be submitted to European Medicines Agency, 7 Westferry Circus, Canary Wharf, London E14 4HB, United Kingdom.

FDA estimates the reporting burden of this common application form as follows. Between January 2000 and May 2006, FDA and EMEA received 226 comparable orphan designation requests/applications of the same drugs for the same diseases or conditions, or an average of 35 per year. With the ease of a common application form, FDA anticipates the number of such requests/applications may increase over time. Therefore, generally there is one request/application per respondent and, at the extreme, all respondents are US-based, FDA believes up to 40 such respondents may use the common application form each year. The respondents will be primarily pharmaceutical companies or other for-profit organizations. For applications submitted exclusively to FDA, we do not believe the new form will result in any increased burden on the respondents and therefore we estimate no additional burden for those respondents. FDA believes the information required for the EMEA submission, for the most part, is very similar to that in the FDA submission, which is already in the respondents' possession. The respondents, however, may have to search existing data sources or gather additional needed data, such as on the prevalence or the availability of alternative methods of diagnosis, prevention, and treatment of the rare disease or condition of interest in the European Community, to complete the EMEA submission. FDA estimates that it will take an additional 32 hours—16 hours of professional time and 16 hours of support time—to compile information required for the EMEA submission. Hence, the estimated total annual human resource hours, at most, would be 1,280 hours for the EMEA submission.

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

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section and FDA Form	Annual No. of Respondents	Annual Frequency per 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
316.20, 316.21, 316.26 Form FDA 3671	40	1	40	32	1,280
316.22	30	1	30	2	60
316.30	500	1	500	2	1,000
316.36	.2	3	.6	15	9
Total					47,559

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

Please note that in January 2008, the FDA Web site is expected to transition to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. After the transition date, electronic submissions will be accepted by FDA through the FDMS only. When the exact date of the transition to FDMS is known, FDA will publish a **Federal Register** notice announcing that date.

Dated: January 7, 2008.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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