4164-01-P

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**[Docket No. FDA-2023-N-1929]**

# Agency Information Collection Activities; Submission for Office of Management and Budget Review; Comment Request; Orphan Drugs

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA, Agency, or we) 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:** Submit written comments (including recommendations) 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 submitted to https://www.reginfo.gov/public/do/PRAMain. Find this particular information collection by selecting "Currently under Review--Open for Public Comments" or by using the search function. The OMB control number for this information collection is 0910-0167. Also include the FDA docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, 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--21 CFR Part 316

OMB Control Number 0910-0167--Extension

This information collection helps support implementation of sections 525, 526, 527, and 528 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360aa, 360bb, 360cc, and 360dd), as well as related guidance and Agency forms. Sections 525, 526, 527, and 528 of the FD&C Act pertain to the development of drugs for rare diseases or conditions, including biological products and antibiotics, otherwise known or referred to as "orphan drugs." Specifically, section 525 of the FD&C Act requires written recommendations on studies required for approval of a marketing application for a drug for a rare disease or condition. Section 526 of the FD&C Act provides for designation of drugs as orphan drugs when certain conditions are met; section 527 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 7 years; and, finally, section 528 is intended 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.

Agency regulations in part 316, subpart A (21 CFR part 316, subpart A) (§§ 316.1 through 316.4) identify the scope of coverage, applicable definitions, and statutory provisions applicable to orphan drugs. The regulations in part 316, subpart B (§§ 316.10 through 316.14) set forth content and format elements for written recommendation requests and discuss FDA providing or refusing to provide the requested written recommendations. Similarly, regulations in part 316, subpart C (§§ 316.20 through 316.30) prescribe content and format elements for requesting orphan drug designation; identify submission schedules for requisite information including amendments, updates, and reports; and provide for publication and revocation of orphan drug designation. Regulations in part 316, subparts D and E (§§ 316.31 through 316.40) address orphan drug exclusive approval and open protocols for investigations, respectively.

Finally, regulations in part 316, subpart F (§§ 316.50 through 316.52) provide for the issuance of guidance documents that apply to the orphan drug provisions of the FD&C Act and regulations in part 316. The list is maintained on the internet and guidance documents are issued in accordance with our good guidance practices regulation in 21 CFR 10.115, which provide for public comment at any time.

The information collection includes the Agency guidance document entitled "Meetings with the Office of Orphan Products Development: Guidance for Industry, Researchers, Patient Groups, and Food and Drug Administration Staff" (July 2015), available for download at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/meetings-office-orphan-products-development. It provides recommendations to industry, researchers, patient groups, and other stakeholders interested in requesting a meeting, including a teleconference, with the Office of Orphan Products Development (OOPD) on issues related to orphan drug designation requests, humanitarian use device 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. It is also intended to assist OOPD staff in addressing such meeting requests. The guidance describes procedures for requesting, preparing, scheduling, conducting, and documenting such meetings and discusses background information we recommend be included in such requests.

The information collection includes Form FDA 3671, Common EMEA/FDA Application for Orphan Medicinal Product, and Form FDA 4035, FDA Orphan Drug Designation Request Form, intended to benefit sponsors who desire to seek orphan designation of drugs intended for rare diseases or conditions from FDA. The form is a simplified method for sponsors to provide only the information required by § 316.20 for FDA decision making. Orphan drug designation requests and related submissions (amendments, annual reports, etc.), humanitarian use device

designation, and rare pediatric disease designation requests and submissions may be submitted electronically by email to the OOPD.

As communicated on our website at https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/designating-orphan-product-drugs-and-biological-products, respondents may submit orphan drug designation requests electronically through the Center for Drug Evaluation and Research (CDER) NextGen portal, or by emailing the required information to orphan@fda.hhs.gov; or by mailing the required information to the OOPD at the address found on our website. New users of the CDER NextGen Portal must register for an account. For designation requests submitted by email, the Agency recommends using automated read receipt to verify receipt of the email.

Sponsors and others who plan to email information to FDA that is private, sensitive, proprietary, or commercial confidential are strongly encouraged to send it from an FDA-secured email address so the transmission is encrypted. The Agency will assume the addresses of emails received or email addresses provided as a point of contact are secure when responding to those email addresses. Sponsors and others can establish a secure email address link to FDA by sending a request to SecureEmail@fda.hhs.gov. There may be a fee to a commercial enterprise for establishing a digital certificate before encrypted emails can be sent to FDA.

Respondents to the information collection are sponsors who develop investigational drugs and biologicals for commercial use and who seek orphan drug designation, and upon approval or licensure, orphan drug exclusivity.

In the *Federal Register* of June 13, 2023 (88 FR 38513), we published a 60-day notice soliciting comment on the proposed collection of information. Although we received one comment, it was not responsive to the information collection topics solicited and therefore is not addressed in this notice.

We estimate the burden of this collection of information as follows based on data from 2022:

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

| 21 CFR Part or Section; Activity | No. of Respondents | No. of Records per Recordkeeper | Total Annual Records | Average Burden per Record | Total Hours |
|---|---|---|---|---|---|
| Part 316 associated records | 780 | 1.25 | 975 | 135 | 131,625 |
| §§ 316.20, 316.21, 316.26 (Form FDA 4035) | 780 | 1.25 | 975 | 32 | 31,200 |
| § 316.22; Notifications of changes in agents | 300 | 1 | 300 | 0.5 | 150 |
| § 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 | 90 | 1 | 90 | 3 | 270 |
| § 316.30; Annual reports | 2,039 | 1 | 2,039 | 3 | 6,117 |
| § 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 | 807 | 1.5 | 1,211 | 4 | 4,842 |
| Total | | | 5,613 | | 174,289 |

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

Our burden estimate includes those activities related to: (1) requesting orphan drug designation; (2) responding to deficiencies letters with submissions of amendments; (3) keeping files current with contact information for agents and transfer of ownership, when applicable; (4) submitting annual reports while products have designation status; and (5) requesting and preparing for both informal and formal meetings. Because the PRA defines a recordkeeping requirement to include reporting those records to the Federal government, we account for these activities cumulatively in table 1 above. Upon a recent evaluation of the information collection, we adjusted our burden estimate to reflect an overall increase of 50,616 hours and an increase of 766 records annually. We attribute this adjustment to an increase in the number of submissions, amendments, and annual reports.

**Dated:** November 29, 2023.

**Lauren K. Roth,**

*Associate Commissioner for Policy.*

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