



This document is scheduled to be published in the Federal Register on 03/11/2016 and available online at <http://federalregister.gov/a/2016-05491>, and on FDsys.gov

4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-0268]

Agency Information Collection Activities; Submission for Office of Management and Budget

Review; Comment Request; Guidance for Industry on Individual Patient Expanded Access

Applications: Form FDA 3926

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.

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-New and title "Individual Patient Expanded Access Applications: Form FDA 3926." 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.

Guidance for Industry on Individual Patient Expanded Access Applications: Form FDA 3926--

OMB Control Number 0910-NEW

I. Background

In the Federal Register of February 10, 2015 (80 FR 7318), FDA announced the availability of a draft guidance for industry entitled “Individual Patient Expanded Access Applications: Form FDA 3926.” In the draft guidance, FDA provided draft Form FDA 3926 (Individual Patient Expanded Access--Investigational New Drug Application (IND)) at Appendix 1 and described this draft form, which FDA stated it intended to make available for licensed physicians to use for expanded access requests for individual patient INDs as an alternative to Form FDA 1571 (Investigational New Drug Application (IND)).

As described in the final guidance, Form FDA 3926 provides a streamlined means to request expanded access to an investigational drug outside of a clinical investigation, or to an approved drug where availability is limited by a risk evaluation and mitigation strategy (REMS), for an individual patient who has a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition. Form FDA 3926 may also be used for certain followup submissions to an individual patient expanded access IND.

FDA may permit expanded access to an investigational new drug outside of a clinical investigation, or to an approved drug where availability is limited by a REMS, for an individual patient when the applicable criteria in § 312.305(a) (21 CFR 312.305(a)) (which apply to all types of expanded access) and the criteria in § 312.310(a) (21 CFR 312.310(a)) (which apply

specifically to individual patient expanded access, including for emergency use) are met. The physician may satisfy some of the submission requirements by referring to information in an existing IND, ordinarily the one held by the investigational drug's manufacturer, if the physician obtains permission from that IND holder. If permission is obtained, the physician should then provide to FDA a letter of authorization (LOA) from the existing IND holder that permits FDA to reference that IND.

Section 312.305(b) sets forth the submission requirements for all types of expanded access requests. One of the requirements under § 312.305(b)(2) is that a "cover sheet" must be included "meeting the requirements of § 312.23(a)." This provision applies to several types of submissions under 21 CFR part 312, ranging from commercial INDs under § 312.23 that involve large groups of patients enrolled in clinical trials to requests from physicians to use an investigational drug for an individual patient. Form FDA 1571 is currently used by sponsors for all types of IND submissions to meet the requirements in § 312.23(a). FDA intends to accept submission of a completed Form FDA 3926 to comply with the IND submission requirements in §§ 312.23, 312.305(b), and 312.310(b). FDA intends to consider a completed Form FDA 3926 with the box in Field 10 checked and the form signed by the physician to be a request in accordance with § 312.10 for a waiver of any additional requirements in part 312 for an IND submission, including additional information currently provided in Form FDA 1571 and Form FDA 1572 (Statement of Investigator, which provides the identity and qualifications of the investigator conducting the clinical investigation).

Under § 312.310(d), in an emergency situation that requires the patient to be treated before a written submission can be made, the request to use the investigational drug for individual patient expanded access may be made by telephone (or other rapid means of

communication) to the appropriate FDA review division. Authorization of the emergency use may be given by an FDA official over the telephone, provided the physician explains how the expanded access use will meet the requirements of §§ 312.305 and 312.310 and agrees to submit an expanded access application within 15 working days of FDA's initial authorization of the expanded access use (§ 312.310(d)). The physician may choose to use Form FDA 3926 for the expanded access application.

As explained in the instructions for Form FDA 3926, the following information would be submitted to FDA by those using Form FDA 3926:

- Initials for the patient and date of submission.
- Type of submission (initial or followup submission).
- Clinical information, including indication, brief clinical history of the patient (age, gender, weight, allergies, diagnosis, prior therapy, response to prior therapy), and the reason for requesting the proposed treatment, including an explanation of why the patient lacks other therapeutic options.
- Treatment information, including the investigational drug's name and the name of the entity supplying the drug (generally the manufacturer), the applicable FDA review division (if known), and the treatment plan. This should include the planned dose, route and schedule of administration, planned duration of treatment, monitoring procedures, and planned modifications to the treatment plan in the event of toxicity.
- LOA, generally obtained from the entity that is the sponsor of the IND (e.g., commercial sponsor/drug manufacturer) being referenced, if applicable.

- Physician's qualification statement. An appropriate statement includes medical school attended, year of graduation, medical specialty, state medical license number, current employment, and job title. Alternatively, the relevant portion of the physician's curriculum vitae may be attached.
- Physician's contact information, including name, physical address, email address, telephone number, facsimile number, and physician's IND number, if previously issued by FDA.
- Contents of submission (for followup/additional submissions), including the type of submission being made. FDA intends to accept Form FDA 3926 for certain followup/additional submissions, which include the following: Initial Written IND Safety Report (§ 312.32(c)); Follow-up to a Written IND Safety Report (§ 312.32(d)); Annual Report (§ 312.33); Summary of Expanded Access Use (treatment completed) (§ 312.310(c)(2)); Change in Treatment Plan (§ 312.30); General Correspondence or Response to FDA Request for Information (§ 312.41); and Response to Clinical Hold (§ 312.42(e)).
- Request for authorization to use Form FDA 3926 for individual patient expanded access application.
- Signature of the physician certifying that treatment will not begin until 30 days after FDA receives the completed application and all required material unless the submitting physician receives earlier notification from FDA that the treatment may proceed. The physician agrees not to begin or continue clinical investigations covered by the IND if those studies are placed on clinical hold. The physician also certifies that informed consent will be obtained in compliance with Federal

requirements (including FDA's regulations in 21 CFR part 50) and that an institutional review board (IRB) that complies with all Federal requirements (including FDA's regulations in 21 CFR part 56) will be responsible for initial and continuing review and approval of the expanded access use. The physician also acknowledges that in the case of an emergency request, treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within 5 working days of treatment. The physician agrees to conduct the investigation in accordance with all other applicable regulatory requirements.

In the Federal Register of February 10, 2015 (80 FR 7318), FDA published a 60-day notice requesting public comment on the proposed collection of information. Twelve comments were received. However, FDA received no comments concerning the accuracy of FDA's estimate of the burden of the proposed collection of information. FDA received several comments on ways to enhance the quality, utility, and clarity of FDA Form 3926 through, for example, the addition of instructions for completing the form and use of the form for certain followup submissions.

(Comment 1) Five comments requested instructions, clarification, or directions concerning the use and submission of Form FDA 3926.

(Response) FDA updated instructions based on information originally included in the draft guidance that will be provided in conjunction with final Form FDA 3926. Clarifying language on form fields has been added to the instructions and the guidance.

(Comment 2) One comment asked for clarification regarding Field 1 of Form FDA 3926 to indicate that the requesting physician should provide this information (not the patient).

(Response) Clarification on Field 1 has been added to the form instructions to state that the patient need not initial the form. This is to indicate that the requesting physician should enter the patient's initials.

(Comment 3) One comment stated that the information requested in Field 3 of draft Form FDA 3926 could become lengthy to complete and asked if a PDF could be attached to the form to provide this information.

(Response) This information is now requested in Field 5. Field 5 has been enlarged to accommodate more handwritten information. The space also has been updated to allow expansion when information is entered electronically in the fillable PDF. Clarifying language has been added to the form and instructions.

(Comment 4) Three comments requested electronic submission capability to expedite applications.

(Response) FDA is determining whether electronic submissions are feasible. FDA intends to provide additional information via its Web site should this become an option.

(Comment 5) Several comments concerned the use of FDA Form 3926 for followup submissions. One comment suggested that FDA develop a new form for followup submissions (rather than requiring the use of Form FDA 1571). Three comments asked that instructions be developed for ongoing patient reporting (i.e., followup submissions).

(Response) FDA has revised the guidance, instructions, and Form FDA 3926 so that the form may be used instead of Form FDA 1571 for certain followup submissions to an existing single patient expanded access IND. Form FDA 3926, the instructions, and the guidance identify the types of followup submissions that qualify and provide additional information on how to use Form FDA 3926 for such submissions.

II. Burden Estimate

As discussed previously in this document, Form FDA 3926 will be available for licensed physicians to use as a streamlined means to request expanded access to an investigational drug outside of a clinical investigation, or to an approved drug where availability is limited by a REMS, for an individual patient who has a serious or immediately life-threatening disease or condition and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition, and to submit certain followup reports. One of the requirements under § 312.305(b)(2) is that a “cover sheet” must be included “meeting the requirements of § 312.23(a).” This provision applies to several types of submissions under part 312, ranging from commercial INDs under § 312.23 that involve large groups of patients enrolled in clinical trials to requests from physicians to use an investigational drug for an individual patient. Form FDA 1571 is currently used by sponsors for all types of IND submissions. However, FDA is concerned that physicians requesting expanded access for an individual patient may have encountered difficulty in completing Form FDA 1571 and the associated documents because the form is not tailored to requests for individual patient expanded access.

The submission requirements for all types of expanded access requests for investigational drugs are provided under § 312.305(b) of FDA’s expanded access regulations. Additional submission requirements for individual patient expanded access requests are provided under § 312.310(b), and the requirements for requesting individual patient expanded access for emergency use are provided under § 312.310(d). FDA currently has OMB approval under control number 0910-0014 for individual patient expanded access information collection under §§ 312.305(b), 312.310(b), and 312.310(d). The submission requirements concerning the use of

Form FDA 3926 for certain followup reports are provided under §§ 312.32(c), 312.32(d), 312.33, 312.310(c)(2), 312.30, 312.41, and 312.42(e).

The estimates for “number of respondents,” “number of responses per respondent,” and “total annual responses” were obtained from the Center for Drug Evaluation and Research (CDER) reports and data management systems and from other sources familiar with the number of submissions received for individual patient expanded access use under part 312. The estimates for “average burden per response” were based on information provided by CDER and other Department of Health and Human Services personnel who are familiar with preparing and reviewing expanded access submissions by practicing physicians.

Based on data for the number of submissions to FDA during 2011, 2012, and 2013, we originally estimated that approximately 790 licensed physicians would use Form 3926 to submit 1.46 requests per physician (respondent) for individual patient expanded access, for a total of 1,153 responses annually. In response to comments received, FDA clarifies in the final guidance and in the form instructions that licensed physicians may also use Form FDA 3926 for certain followup submissions. Based on data for the number of followup submissions during 2011, 2012, and 2013, FDA estimates that about 790 physicians will each use Form FDA 3926 to submit 1.57 followup submissions per physician, for approximately 1,241 followup responses annually. Based on these estimates, FDA calculates the total annual responses to be 2,394 (1,153 requests for individual patient expanded access and 1,241 followup submissions) by 790 physicians for an average of 3.03 responses per respondent. FDA estimates the average burden per response to be 45 minutes (0.75 hour). Based on this estimate, FDA calculates the total burden to be 1,795 hours. Under OMB control number 0910-0014, FDA currently has OMB

approval of 17,592 hours for these submissions. The use of FDA Form 3926 will reduce the current burden by 15,797 hours.

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

Table 1.--Estimated Annual Reporting Burden¹

Guidance on Individual Patient Expanded Access Applications: Form FDA 3926	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Expanded access submission for treatment of an individual patient, including submission of Form FDA 3926	790	3.03	2,394	0.75 (45 minutes)	1,795

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

Dated: March 8, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-05491 Filed: 3/10/2016 8:45 am; Publication Date: 3/11/2016]