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

OMB Control No. 0910-NEW

SUPPORTING STATEMENT

Terms of Clearance: None.

A. Justification

1. Circumstances Making the Collection of Information Necessary

The authorizing statute for this information collection is 21 U.S.C. 360bbb (see also 21 CFR part 312). Submission requirements for individual patient expanded access are provided under 21 CFR 312.310.

FDA may permit expanded access to an investigational new drug for an individual patient when the applicable criteria in § 312.305(a) (which apply to all types of expanded access) and the criteria in § 312.310(a) (which apply specifically to individual patient expanded access, including for emergency use) are met.

Section 312.305(b) sets forth the submission requirements for all types of expanded access requests. Section 312.310(b) contains additional submission requirements for individual patient expanded access requests made by a licensed physician, and § 312.310(d) contains the requirements for requesting individual patient expanded access for emergency use. FDA currently has approval under OMB control number 0910-0014 for individual patient expanded access information collection under §§ 312.305(b), 312.310(b), and 312.310(d).

Under § 312.310(b), the expanded access submission must include information adequate to demonstrate that the criteria for all expanded access uses and those specific to individual patient expanded access have been met.

Section 312.310(b)(1) states that if the drug is the subject of an existing investigational new drug application (IND), the expanded access submission may be made by a licensed physician.

Section 312.310(b)(3) states that a licensed physician may satisfy some of the submission requirements by obtaining a right of reference to pertinent information in an existing IND and by providing any other required information not contained in the IND (usually only the information specific to the individual patient).

Section 312.305(b)(1) states that an expanded access submission is required for each type of expanded access. The submission may be a new IND or a protocol amendment to an existing IND. Information required for a submission may be supplied by referring to

pertinent information contained in an existing IND if the sponsor of the existing IND grants a right of reference to the IND.

Section 312.305(b)(2) describes the expanded access submission requirements. The following items must be included:

- A cover sheet (currently Form FDA 1571 -- Investigational New Drug Application (IND)) meeting the requirements of § 312.23(a);

- The rationale for the intended use of the drug, including a list of available therapeutic options that will ordinarily be tried before resorting to the investigational drug, or an explanation of why the use of the investigational drug is preferable to the use of available therapeutic options;

- The criteria for patient selection or, for an individual patient, a description of the patient's disease or condition, including recent medical history and previous treatments used for the disease or condition;

- The method of administration of the drug, dose, and duration of therapy;

- A description of the facility where the drug will be manufactured;

- Chemistry, manufacturing, and controls information adequate to ensure the proper identification, quality, purity, and strength of the investigational drug;

- Pharmacology and toxicology information adequate to conclude that the drug is reasonably safe at the dose and duration proposed for expanded access use (ordinarily, information that will be adequate to permit clinical testing of the drug in a population of the size expected to be treated); and

- A description of clinical procedures, laboratory tests, or other monitoring necessary to evaluate the effects of the drug and minimize its risks.

One of the requirements under § 312.305(b)(2) is that a "cover sheet" 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 providing the associated documents because Form FDA 1571 is not tailored to requests for individual patient expanded access.

FDA developed Form FDA 3926 (Individual Patient Expanded Access -- Investigational New Drug Application (IND)) 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 Risk Evaluation and Mediation 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 requests the following information:

- Initials for the patient and date of submission.

- Type of submission (initial or follow-up 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.

- Letter of authorization (LOA), generally obtained from the entity that is the sponsor of the IND (e.g., commercial sponsor/drug manufacturer) being referenced, should be attached, 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 follow-up/additional submissions), including the type of submission being made. FDA intends to accept Form FDA 3926 for certain follow-up/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 to comply with the requirements for an 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 materials unless the submitting physician receives earlier notification from FDA that the treatment may begin. 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 Federal IRB 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.

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 ordinarily 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.

2. Purpose and Use of the Information Collection

This ICR collects information from licensed physicians who wish to submit a request for expanded access to an investigational drug outside of a clinical investigation, or to an approved drug where availability is limited by 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. This information is collected through the use of new Form FDA 3926 (Individual Patient Expanded Access -- Investigational New Drug Application (IND)), which FDA

developed for licensed physicians to use as a streamlined alternative to Form FDA 1571 (Investigational New Drug Application (IND)). Physicians may use Form FDA 3926 instead of Form FDA 1571 for the submission of information as described in FDA regulations -- for example, the rationale for the intended use of the drug and the physician's qualifications. FDA will use the information to determine if the expanded access request is allowed to proceed or if the application will be put on clinical hold. Form FDA 3926 may also be used for certain follow-up submissions to existing individual patient expanded access INDs as described in FDA regulations -- for example, to submit an annual report or summary of expanded access use (treatment completed).

3. Use of Improved Information Technology and Burden Reduction

   Form FDA 3926 will be available as a fillable PDF document. FDA estimates that 95 percent of respondents will use the fillable features of this form. FDA is determining whether direct electronic submissions of the completed form are feasible. FDA intends to provide additional information via its Web site should direct electronic submissions become an option.

4. Efforts to Identify Duplication and Use of Similar Information

   Form FDA 3926 is available as an alternative to Form FDA 1571 and reduces the burden associated with the collection of information for individual patient expanded access submissions currently approved under OMB control number 0910-0014. This collection of information does not duplicate any other submission to FDA. FDA is the only agency that requires this information, to FDA's knowledge. There is no similar information available from any other source.

5. Impact on Small Businesses or Other Small Entities

   The respondents to this information are an estimated 790 licensed physicians annually. Licensed physicians currently submit information for individual patient expanded access through the use of Form FDA 1571, as provided under part 312. FDA is helping licensed physicians minimize the burden for this collection of information through the use of Form FDA 3926, which provides a streamlined alternative for physicians seeking individual patient expanded access and for providing certain follow-up submissions. Form FDA 3926 may be used in place of Form FDA 1571.

6. Consequences of Collecting the Information Less Frequently

   The information will be collected once for initial requests and occasionally for follow-up submissions, as described in part 312. Because Form FDA 3926 streamlines the process for requesting expanded access to an investigational drug for an individual patient and for filing certain follow-up submissions to an individual patient expanded access IND, it reduces the previously approved information collection burden associated with the use of Form FDA 1571. Less frequent collection of this information would not provide the necessary information needed by FDA to make appropriate determinations for individual patient expanded access INDs.

   There are no legal obstacles to reduce the burden.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances relating to this information collection.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the Federal Register of 02/10/2015 (80 FR 7318). 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 Form FDA 3926 through, for example, the addition of instructions for completing the form and use of the form for certain follow-up 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 Form FDA 3926 for follow-up submissions. One comment suggested that FDA develop a new form for follow-up submissions (rather than requiring the use of Form FDA 1571). Three comments asked that instructions be developed for ongoing patient reporting (i.e., follow-up 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 follow-up submissions to an existing individual patient expanded access IND. Form FDA 3926, the instructions, and the guidance identify the types of follow-up submissions that qualify and provide additional information on how to use Form FDA 3926 for such submissions.

FDA provided information that clarifies the information submission process and facilitates the use of Form FDA 3926 for initial and follow-up submissions. FDA does not consider the comments to present any issues to be resolved further.

9. Explanation of Any Payment or Gift to Respondents

There is no payment or gift to respondents associated with this guidance.

10. Assurance of Confidentiality Provided to Respondents

The confidentiality of information received by FDA would be handled consistent with the Freedom of Information Act (FOIA) and FDA's published regulations under § 312.130 and 21 CFR part 20.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature applicable to this collection of information.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

As indicated in table 1, the total annual estimated burden for this information collection is 1,795 hours. 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. FDA estimates the information collection burden as follows:

Table 1.--Estimated Annual Reporting Burden

Guidance Section	FDA Form No.	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
Section III: Initial submission for treatment of an individual patient	3926	790	1.46	1,153	0.75 (45 mins.)	865
Section III: Follow-up submissions	3926	790	1.57	1,241	0.75 (45 mins.)	930
TOTAL						1,795

As shown in Table 1, FDA estimates that about 790 physicians will use Form FDA 3926 for 2,394 expanded access submissions (1,153 individual patient expanded access INDs and approximately 1,241 follow-up submissions). Based on these estimates, FDA calculates the total annual responses to be 2,394. Because respondents will complete different fields of the form depending on whether the submission is an initial submission or follow up submission, we believe that the average burden per response to be 45 minutes (0.75 hour), independent of submission type. Based on this estimate, FDA calculates the total burden to be 1,795 hours.

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

12b. Annualized Cost Burden Estimate

The industry burden estimate calculated in section 12a would result in labor costs where the physician hourly wage rate is calculated using the rate reported by the U.S. Department of Labor, Bureau of Labor Statistics, May 2014 National Occupational Employment and Wage Estimates.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Physicians	1,795	$93.74	$168,263

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating, or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

The guidance and form are designed to streamline the information collection required to support individual patient expanded access requests and follow-up submissions. Thus, FDA does not expect a significant increase in current budgeted costs for FDA resulting from this guidance and form because expanded access requests are already submitted to the agency using Form FDA 1571.

FDA staff will review individual patient expanded access requests submitted using Form FDA 3926 to determine if the expanded access request will be allowed to proceed or if the application will be put on clinical hold. The grade level of the staff who perform these reviews ranges from a GS-12 to a GS-14, and it takes approximately one hour cumulative (i.e., combined hours of disciplines involved) to review each submission. The annual cost to the Federal government is approximately $134,159.76.

15. Explanation for Program Changes or Adjustments

This is a new information collection request..

16. Plans for Tabulation and Publication and Project Time Schedule

No tabulation of the data from this information collection is planned for publication.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA is not seeking approval to exempt the display of the expiration date of the OMB approval. The OMB expiration date will be displayed on the form where required.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.