Foreign Clinical Studies Not Conducted Under an
Investigational New Drug Application
(0910-0622)
SUPPORTING STATEMENT

Terms of Clearance: None

A. Justification

1. Circumstances Making the Collection of Information Necessary

Previous § 312.120 (21 CFR 312.120) stated that we generally accept foreign clinical studies not conducted under an IND provided they are well designed, well conducted, performed by qualified investigators, and conducted in accordance with ethical principles. It further stated that such studies must be conducted in accordance with the 1989 Declaration of Helsinki (1989 Declaration) or the laws of the country in which the research is conducted, whichever provides greater protection to subjects.

Under current § 312.120, FDA accepts foreign clinical studies not conducted under an IND as support for an IND or application for marketing approval for a drug or biological product if the studies are conducted in accordance with good clinical practices (GCP), including review and approval by an independent ethics committee (IEC).

Under § 312.120(a), FDA accepts as support for an IND or application for marketing approval a well-designed and well-conducted foreign clinical study not conducted under an IND if the study is conducted in accordance with GCP, and we are able to validate the data from the study through an onsite inspection if necessary. GCP includes review and approval by an IEC before initiating a study, continuing review of an ongoing study by an IEC, and obtaining and documenting the freely given informed consent of the subject before initiating a study.

Under § 312.120(b), a sponsor of a non-IND foreign study who wants to rely on that study as support for an IND or application for marketing approval must provide the following information to FDA: (1) The investigator's qualifications; (2) a description of the research facilities; (3) a detailed summary of the protocol and results of the study and, should FDA request, case records maintained by the investigator or additional background data such as hospital or other institutional records; (4) a description of the drug substance and drug product used in the study, including a description of the components, formulation, specifications, and, if available, bioavailability of the specific drug product used in the clinical study; (5) if the study is intended to support the effectiveness of a drug product, information showing that the study is adequate and well controlled under Sec. 314.126; (6) the name and address of the IEC that reviewed the study and a statement that the IEC meets the definition in Sec. 312.3; (7) a summary of the IEC's decision to approve or modify and approve the study, or to provide a favorable opinion; (8) a description of how informed consent was obtained; (9) a description of what incentives, if any, were provided to subjects to participate in the study; (10) a description of how the sponsor(s) monitored the study and ensured that the study was carried out consistently with the study protocol; and (11) a description of how investigators were trained to comply with GCP and to conduct the study in accordance with the study protocol, and a statement on whether written commitments by investigators to comply with GCP and the protocol were obtained.

Section 312.120(c) specifies how sponsors or applicants can request a waiver for any of the requirements under § 312.120(a)(1) and (b). Under § 312.120(c)(1), a waiver request must contain at least one of the following: (1) An explanation why the sponsor's or applicant's

compliance with the requirement is unnecessary or cannot be achieved, (2) a description of an alternative submission or course of action that satisfies the purpose of the requirement, or (3) other information justifying a waiver.

2. Purpose and Use of the Information Collection

Under § 312.120, FDA accepts foreign clinical studies not conducted under an IND as support for an IND or application for marketing approval for a drug or biological product if the studies are conducted in accordance with GCP, including review and approval by an independent ethics committee IEC.

3. Use of Improved Information Technology and Burden Reduction

FDA has developed several guidances for industry to improve the use of information technology in the submission of marketing applications for human drugs and related reports. These guidance documents and others are available at FDA's web site http://www.fda.gov/cder/guidance/index.htm.

4. Efforts to Identify Duplication and Use of Similar Information

This information is not otherwise submitted to the agency, and thus, there is no duplicate reporting.

5. Impact on Small Businesses or Other Small Entities

As explained in the "Analysis of Economic Impacts" section of the final rule amending § 312.120 (73 FR 22800), this requirement is unlikely to have a significant impact on a substantial number of small entities.

6. Consequences of Collecting the Information Less Frequently

Section 312.120 is intended to update the standards for the acceptance of foreign clinical

studies not conducted under an IND and to help ensure the protection of human subjects and the quality and integrity of data obtained from these studies.

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

There are no special circumstances for this collection of information.

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 February 26, 2013 (78 FR 13067). No comments were received that pertained to the collection of information.

9. Explanation of Any Payment or Gift to Respondents

FDA did not provide any payment or gifts to respondents.

10. Assurance of Confidentiality Provided to Respondents

The release of information submitted to FDA under an IND is governed by the provisions of 21 CFR 312.5 and 314.430. In general, these provisions do not permit public disclosure of

information in IND files unless that information has previously been publicly disclosed. Confidentiality of information submitted for an NDA is protected under 21 CFR 314.430 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 310(j) of the Federal Food, Drug, and Cosmetic act.

11. Justification for Sensitive Questions

No questions of a sensitive nature are asked.

12. Estimates of Annualized Hour Burden and Costs

12a. Annualized Hour Burden Estimate

We estimate that 237 companies will submit a total of approximately 1,185 non-IND foreign clinical studies in support of an IND or application for marketing approval for a drug or biological product. Hour burden estimates vary due to differences in size, complexity, and duration across studies, and we estimate that complying with § 312.120 would take sponsors between 18 and 32 hours annually for each non-IND foreign clinical trial, totaling 37,920 hours (32 x 1,185).

A waiver request may be submitted in an IND or in an information amendment to an IND, or in an application or in an amendment or supplement to an application submitted under 21 CFR part 314 or 601. Section 312.10 sets forth requirements for sponsors who request waivers from FDA for compliance with any of the provisions in part 312, and § 314.90 sets forth requirements for applicants who request waivers from FDA for compliance with §§ 314.50 through 314.81. FDA has approval for the submission of these waiver requests under OMB control numbers 0910-0014 for part 312 and 0910-0001 for part 314.

In addition to the reporting requirements set forth in table 1 of this document, there is also a recordkeeping provision in § 312.120(d) stating how long sponsors and applicants must retain records required by § 312.120. In addition, § 312.120(b) states that any signed written commitments by investigators must be maintained by the sponsor or applicant and made

available for FDA review upon request, and also specifies sponsor recordkeeping of IEC-related information. Under § 312.120(d), if a study is submitted in support of an application for marketing approval, records must be retained for 2 years after an Agency decision on that application; if a study is submitted in support of an IND but not an application for marketing approval, records must be retained for 2 years after the submission of the IND. The retention requirements in § 312.57(c) for records and reports required under part 312 apply to these provisions, and are approved under OMB control number 0910-0014.

The estimated annual reporting burden for this request for OMB approval is as follows:

Table 1.—Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
312.120	237	5	1,185	32	37,920

12b. Annualized Cost Burden Estimates

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Pharmaceutical/Biological	37,920	$75.00	$2,844,000

13. Estimates of Other Total Annual Cost Burden to Respondents and 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

There are no additional cost burdens to FDA to review these submissions. These reviews are already accounted for in the Federal burden estimates for OMB Control Numbers 0910-0001, 0910-0014, and 0910-0338.

15. Explanation for Program Changes or Adjustments

The burden estimates approved by the Office of Management and Budget in the April 28,

2008 final rule have been updated by FDA's Economics Staff to reflect current burdens.

16. Plans for Tabulation and Publication and Project Time Schedule

Information collected under this requirement will not be published.

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

The agency does not seek an exemption from displaying the expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.