Investigational New Drug (IND) Safety Reporting Requirements
for Human Drug and Biological Products and Safety Reporting
Requirements for Bioavailability and Bioequivalence Studies in Humans

OMB Control No. 0910-0672

SUPPORTING STATEMENT

A. Justification

1. Circumstances Making the Collection of Information Necessary

In the Federal Register of September 29, 2010 (75 FR 59960), FDA published a final rule entitled "*Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans*." The rule clarified the agency's expectations for timely review, evaluation, and submission of relevant and useful safety information and implemented internationally harmonized definitions and reporting standards for Investigational New Drug (IND) safety reports. The rule also required safety reporting for bioavailability and bioequivalence studies. The rule was intended to improve the utility of IND safety reports, expedite FDA's review of critical safety information, better protect human subjects enrolled in clinical trials, and harmonize safety reporting requirements internationally.

As a result of the rulemaking FDA regulations were revised to include additional reporting requirements. These revisions are reflected in 21 CFR parts 312 and 320. Because these provisions may be incorporated into the currently approved information collection provisions found in OMB Control Nos. 0910-0014 *Investigational New Drug Regulations* and 0910-0291 *MedWatch: FDA Medical Products Reporting Program*, respectively, the agency will revise those collections accordingly. In the interim, FDA is requesting OMB approval of the instant information collection provisions found in the following regulations:

21 CFR 312.32(c)(1)(ii) and (c)(1)(iii); section 312.32(c)(1)(ii) requires reporting to FDA, in an IND safety report, of potential serious risks from clinical trials within 15 calendar days for findings from epidemiological studies, pooled analyses of multiple studies, or other clinical studies that suggest a significant risk in humans exposed to the drug. Section 312.32(c)(1)(iii) specifies the requirements for reporting to FDA in an IND safety report potential serious risks from clinical trials within 15 calendar days for findings from in vitro testing that suggest a significant risk to humans.

21 CFR 312.32(c)(1)(iv) requires reporting to FDA in an IND safety report within 15 calendar days of any clinically important increase in the rate of occurrence of serious suspected adverse reactions over that listed in the protocol or investigator brochure.

21 CFR 320.31(d) requires mandatory safety reporting for bioavailability and bioequivalence studies on Form FDA 3500A (approved under OMB Control No. 0910-0291) or other electronic format FDA can process.

2. Purpose and Use of the Information Collection

The information collection is intended to improve the utility of IND safety reports, expedite FDA's review of critical safety information, better protect human subjects enrolled in clinical trials, and harmonize safety reporting requirements internationally.

3. Use of Improved Information Technology and Burden Reduction

Information collection is conducted electronically through agency-supported technology.

4. Efforts to Identify Duplication and Use of Similar Information

The information collection reflects burden that would otherwise be captured under OMB Control Nos. 0910-0014, *Investigational New Drug Regulations* and 0910-0291, *MedWatch: FDA's Medical Products Reporting Program*. FDA will incorporate the burden under the instant collection into these collections accordingly.

5. Impact on Small Businesses or Other Small Entities

While the information collection provisions apply to small and large businesses alike, FDA aids small businesses in complying with its requirements through the agency's Regional Small Business Representatives and through the scientific and administrative staffs within the agency. FDA has provided a Small Business Guide on the agency's website at http://www.fda.gov/oc/industry/.

6. Consequences of Collecting the Information Less Frequently

The reporting frequency is prescribed in accordance with the Federal Food, Drug, and Cosmetic Act regarding the safety of human subjects in clinical studies. FDA must have information about studies before they begin. Also, in monitoring the progress of ongoing studies, FDA needs timely information on serious adverse effects and significant new information derived from animal studies, from foreign marketing experience, and other study data. Less frequent reporting increases the potential risk to human health and exposure to unsafe drugs.

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

The agency's IND regulations require more than a quarterly reporting schedule (21 CFR 312.32) to ensure expedited FDA review of product applications. At the same time, FDA feels these reporting requirements impose the minimum burden necessary while allowing us to make informed determinations of safety and effectiveness.

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 March 18, 2016 (81 FR 14860). No comments were received in response to the notice.

9. Explanation of Any Payment or Gift to Respondents

No payment or gift is made to respondents to the information collection.

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. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the act.

11. Justification for Sensitive Questions

The information collection contains no questions of a sensitive nature.

12. Estimates of Annualized Hour Burden and Costs

Description of Respondents: Respondents to the collection are businesses or other "for-profit" organizations sponsoring IND applications, or anyone otherwise subject to 21 CFR parts 312 and 320.

We estimate the burden of the information collection as follows:

12a. Annualized Hour Burden Estimate

Table 1 – CDER Estimated Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
320.31(d) Bioavailability and Bioequivalence Safety Reports	13	15	195	14	2,730
312.32(c)(1)(ii) and (c)(1)(iii) IND Safety Reports	100	6	600	12	7,200
312.32(c)(1)(iv) IND Safety Reports	10	1	10	12	120
TOTAL	123		805		10,050

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

Table 2 – CBER Estimated Annual Reporting Burden[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Avg. Burden per Response	Total Hours
320.31(d) Bioavailability and Bioequivalence Safety Reports	1	1	1	14	14
312.32(c)(1)(ii) and (c)(1)(iii) IND Safety Reports	137	4	548	12	6,576
312.32(c)(1)(iv) IND Safety Reports	5	1.4	7	12	84
TOTAL	143		556		6,674

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

12b. Annualized Cost Burden Estimate

Costs to respondents are reflected in currently approved collections 0910-0014 and 0910-0291. FDA will consolidate the annual hourly burden associated with the instant collection accordingly.

13. Estimates of Other Total Annual Cost Burden 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

Cost of the information collection is absorbed under currently allocated resources.

15. Explanation for Program Changes or Adjustments

The burden reflects an increase FDA attributes to an increase in the number of respondents and submissions as a result of the reporting requirements in the the rulemaking for the underlying regulations. Specifically we have included **551** additional responses and **6,604** additional hours. We have also eliminated the estimated costs previously included as we believe these were realized upon implementation of the rule which became effective March 28, 2011. Before expiration of the instant collection, burden associated with provisions under 21 CFR part 312 will be consolidated into OMB Control No. 0910-0014, *Investigational New Drug Regulations*; and burden associated with provisions under 21 part 320 will be consolidated into OMB Control No. 0910-0291, *MedWatch: FDA's Medical Products Reporting Program*. The agency plans to revise these collections accordingly.

16. Plans for Tabulation and Publication and Project Time Schedule

The agency has no plans for any publication regarding the information collection.

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

Display is appropriate.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.