



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-N-0663]

Agency Information Collection Activities; Proposed Collection; Comment Request;

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

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal Agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans.

DATES: Submit either electronic or written comments on the collection of information by

[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: You may submit comments as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <http://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <http://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2013-N-0663 for "Investigational New Drug Safety Reporting Requirements for Human Drug and Biological Products and Safety Reporting Requirements for Bioavailability and Bioequivalence Studies in Humans." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <http://www.regulations.gov> or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION". The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <http://www.regulations.gov>. Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <http://www.fda.gov/regulatoryinformation/dockets/default.htm>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: FDA PRA Staff, Office of Operations, Food and Drug Administration, 8455 Colesville Rd., COLE-14526, Silver Spring, MD 20993-0002, PRASStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. "Collection of information" is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the Federal Register concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality,

utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

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

OMB Control Number 0910-0672--Extension

In the **Federal Register** of October 31, 2013 (78 FR 65338), FDA published a document 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 document 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 IND safety reports. The document also required safety reporting for bioavailability and bioequivalence studies. The document was intended to improve the utility of Investigational New Drug (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.

The rulemaking included the following information collection under the PRA that was not already included in 21 CFR 312.32 and approved under OMB control number 0910-0014.

Section 312.32(c)(1)(ii) and (c)(1)(iii) 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.

Section 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.

The rulemaking also included new information collection under the PRA by requiring safety reporting for bioavailability and bioequivalence studies (21 CFR 320.31(d)).

In tables 1 and 2 of this document, the estimates for "No. of Respondents," "No. of Responses per Respondent," and "Total Annual Responses" were obtained from the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) reports and data management systems for submissions received in 2013, 2014, and 2015, and from other sources familiar with the number of submissions received under the noted 21 CFR section. The estimates for "Hours per Response" are unchanged based on information from CDER and CBER individuals familiar with the burden associated with these reports and from prior estimates received from the pharmaceutical industry. FDA estimates the burden of this collection of information as follows:

Table 1.--Estimated Annual Reporting Burden -- (CDER)¹

| 21 CFR section | Number of respondents | Number of responses per respondent | Total annual responses | Average 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 (CDER) | | | | | 10,050 |

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

Table 2.--Estimated Annual Reporting Burden -- (CBER)¹

| 21 CFR section | Number of respondents | Number of responses per respondent | Total annual responses | Average 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 (CBER) | | | | | 6,674 |

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

Dated: March 14, 2016.

Leslie Kux,

Associate Commissioner for Policy.

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