4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2015-D-3327]

Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to International Council for Harmonisation E6(R1)

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA, Agency, or we) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (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 information collection recommendations found in Agency guidance pertaining to the development of a system to manage quality as well as information to include in a clinical study report about the quality management approach.

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. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before

[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. The https://www.regulations.gov electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://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 https://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): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, 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-2015-D-3327 for "Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)." Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff 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 https://www.regulations.gov. Submit both copies to the Dockets Management Staff. 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: https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://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 Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, PRAStaff@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.

Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)

OMB Control Number 0910-0843--Extension

This information collection request supports recommendations found in the Agency guidance entitled "E6(R2) Good Clinical Practice; Integrated Addendum to ICH E6(R1)" (ICH E6(R2). The guidance was originally prepared under the auspices of the International Council for Harmonisation (ICH) (formerly the International Conference on Harmonisation); it amends the ICH guidance for industry entitled "E6 Good Clinical Practice: Consolidated Guidance" (issued in April 1996). The guidance is intended to facilitate implementation of improved and more efficient approaches to clinical trial design, including conduct, oversight, recording, and reporting. This is intended to increase clinical trial quality and efficiency while continuing to ensure human subject protection and reliability of trial results. Included in the guidance are additions identified as "ADDENDUM" and marked with vertical lines on both sides of the text.

Standards regarding electronic records and essential documents intended to increase clinical trial quality and efficiency have also been updated. The guidance is available from our

website at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1.

We estimate the burden of the information collection as follows:

Table 1.--Estimated Annual Recordkeeping Burden for Human Drugs[1]

Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Section 5. Quality Management (including sections 5.0.1 to 5.0.7)--Developing a Quality Management System	1,457	1	1,457	60	87,420

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

Table 2.--Estimated Annual Reporting Burden for Human Drugs[1]

Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Section 5.0.7. Risk Reporting--Describing the Quality Management Approach Implemented in a Clinical Trial and Summarizing Important Deviations From the Predefined Quality Tolerance Limits and Remedial Actions Taken in the Clinical Study Report	1,457	4.6	6,702	3	20,106

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

Table 3.--Estimated Annual Recordkeeping Burden for Biologics[1]

Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)	No. of Recordkeepers	No. of Records per Recordkeeper	Total Annual Records	Average Burden per Recordkeeping	Total Hours
Section 5. Quality Management (including sections 5.0.1 to 5.0.7)--Developing a Quality Management System	423	1	423	60	25,380

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

Table 4.--Estimated Annual Reporting Burden for Biologics[1]

Guidance for Industry on E6(R2) Good Clinical Practice; International Council for Harmonisation; Integrated Addendum to ICH E6(R1)	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Section 5.0.7. Risk Reporting--Describing the Quality Management Approach Implemented in a Clinical Trial and Summarizing Important Deviations From the Predefined Quality Tolerance Limits and Remedial Actions Taken in the Clinical	423	1.56	660	3	1,980

Study Report					

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

In table 1, we estimate 1,457 sponsors of clinical trials of human drugs will develop approximately 1,457 quality management systems per year (as described in ICH E6(R2) in section 5.0, including sections 5.0.1 to 5.0.7). We assume it will take respondents 60 hours to develop and implement each quality management system, totaling 87,420 hours annually. The estimated number of sponsors who will develop a quality management system as described in ICH E6(R2) is based on the number of annual investigational new drug applications (INDs) and new drug applications (NDAs) submitted to FDA's Center for Drug Evaluation and Research. The estimated number of hours we assume it takes to develop a quality management system is based on informal interactions with industry about activities that support drug development plans.

In table 2, we estimate 1,457 sponsors of clinical trials of human drugs will describe the quality management approach implemented in a clinical trial and summarize important deviations from the predefined quality tolerance limits and remedial actions taken in the clinical study report (as described in section 5.0.7 of ICH E6(R2)). We further estimate that sponsors will submit approximately 4.6 responses per respondent and that it will take sponsors 3 hours to complete this reporting task, totaling 20,106 reporting hours annually. These estimates are based on our past experiences with INDs and NDAs.

In table 3, we estimate 423 sponsors of clinical trials of biological products will develop 423 quality management systems per year (as described in ICH E6(R2) in section 5.0, including sections 5.0.1 to 5.0.7). We assume it will take respondents 60 hours to develop and implement each quality management system, totaling 25,380 hours annually. The estimated number of sponsors who will develop a quality management system as described in ICH E6(R2) is based on

the number of annual INDs and biologics license applications (BLAs) submitted to FDA's Center for Biologics Evaluation and Research. The estimated number of hours we assume it takes to develop a quality management system is based on informal interactions with industry about activities that support drug development plans.

In table 4, we estimate 423 sponsors of clinical trials of biological products will describe the quality management approach implemented in a clinical trial and summarize important deviations from the predefined quality tolerance limits and remedial actions taken in a clinical study report (as described in section 5.0.7 of ICH E6(R2)). We further estimate that sponsors will submit approximately 660 responses per respondent and that it will take sponsors 3 hours to complete this reporting task, totaling 1,980 reporting hours annually. As described previously, these estimates are based on past experiences with INDs and BLAs submitted to FDA.

Although our estimated burden for the information collection reflects an overall decrease of 433 hours, we have increased the estimate by 861 records. We are making this adjustment based on an increase in the number of submissions we received over the last few years.

Dated: August 28, 2019.

Lowell J. Schiller,

Principal Associate Commissioner for Policy.

[FR Doc. 2019-19113 Filed: 9/4/2019 8:45 am; Publication Date: 9/5/2019]