

Based on data from the Document Archiving, Reporting and Regulatory Tracking System for the number of submissions to FDA using FDA Form 3926 during fiscal years 2015, 2016, and 2017, we estimate that approximately 790 licensed physicians would use FDA Form 3926 to submit 1.46 requests per physician (respondent) for individual patient expanded access, for a total of 1,153 responses annually. Based on these estimates, FDA calculates the total annual responses to be 2,394 (1,153 requests for individual patient expanded access and 1,241 follow-up submissions) by 790 physicians for an average of 3.03 responses per respondent. FDA estimates the average burden per response to be 45 minutes (0.75 hour). Based on this estimate, FDA calculates the total burden to be 1,795 hours.

Dated: October 31, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018-24321 Filed 11-6-18; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-N-4130]

Agency Information Collection Activities; Proposed Collection; Comment Request; Recordkeeping Requirements for Microbiological Testing and Corrective Measures for Bottled Water

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) 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 the procedure by which both domestic and foreign bottled water manufacturers that sell bottled water in the United States maintain records of microbiological testing and corrective measures, in addition to existing recordkeeping requirements.

DATES: Submit either electronic or written comments on the collection of information by January 7, 2019.

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 January 7, 2019. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of January 7, 2019. 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-2018-N-4130 for "Agency Information

Collection Activities; Proposed Collection; Comment Request; Recordkeeping Requirements for Microbiological Testing and Corrective Measures for Bottled Water." 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, 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.

Recordkeeping Requirements for Microbiological Testing and Corrective Measures for Bottled Water—21 CFR 129.35(a)(3)(i), 129.80(g), and 129.80(h)

OMB Control Number 0910–0658—Extension

The bottled water regulations in parts 129 and 165 (21 CFR parts 129 and 165) require that if any coliform organisms are detected in weekly total coliform testing of finished bottled water, followup testing must be conducted to determine whether any of the coliform organisms are *Escherichia coli* (*E. coli*). The adulteration provision of the bottled water standard (§ 165.110(d)) provides that a finished product that tests positive for *E. coli* will be deemed adulterated under section 402(a)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 342(a)(3)). In addition,

the current good manufacturing practice (CGMP) regulations for bottled water in part 129 require that source water from other than a public water system (PWS) be tested at least weekly for total coliform. If any coliform organisms are detected in the source water, the bottled water manufacturers are required to determine whether any of the coliform organisms are *E. coli*. Source water found to contain *E. coli* is not considered water of a safe, sanitary quality and would be unsuitable for bottled water production. Before a bottler may use source water from a source that has tested positive for *E. coli*, a bottler must take appropriate measures to rectify or otherwise eliminate the cause of the contamination. A source previously found to contain *E. coli* will be considered negative for *E. coli* after five samples collected over a 24-hour period from the same sampling site are tested and found to be *E. coli* negative.

Description of Respondents: The respondents to this information collection are domestic and foreign bottled water manufacturers that sell bottled water in the United States.

We estimate the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

21 CFR section; activity	Number of recordkeepers	Number of records per recordkeeper	Total annual records	Average burden per recordkeeping	Total hours
§§ 129.35(a)(3)(i) and 129.80(h) (bottlers subject to both source water and finished product testing)	319	6	1,914	0.08 (5 minutes) ..	153
§ 129.80(g) and (h) (bottlers only subject to finished product testing).	95	3	285	0.08 (5 minutes) ..	23
§§ 129.35(a)(3)(i) and 129.80(h) (bottlers conducting secondary testing of source water).	3	5	15	0.08 (5 minutes) ..	1
§§ 129.35(a)(3)(i) and 129.80(h) (bottlers rectifying contamination).	3	3	9	0.25 (15 minutes)	2
Total					179

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

Based on a review of the information collection since our last request for OMB approval, we have made no adjustments to our burden estimate.

The current CGMP regulations already reflect the time and associated recordkeeping costs for those bottlers that are required to conduct microbiological testing of their source water, as well as total coliform testing of their finished bottled water products. We therefore conclude that any additional burden and costs in recordkeeping based on followup testing that is required if any coliform

organisms detected in the source water test positive for *E. coli* are negligible.

We estimate that the labor burden of keeping records of each *E. coli* followup test is about 5 minutes per test. We also require followup testing of source water and finished bottled water products for *E. coli* when total coliform positives occur. We expect that 319 bottlers that use sources other than PWSs may find a total coliform positive sample about three times per year in source water testing and about three times in finished product testing and thus would need to conduct six tests for *E. coli*, for a total

of 153 hours of recordkeeping. In addition, about 95 bottlers that use PWSs may find a total coliform positive sample about three times per year in finished product testing and thus would need to conduct three tests for *E. coli*, for a total of 23 hours of recordkeeping.

We expect that three bottlers per year will test positive for *E. coli* in source water and will need to take actions to rectify or eliminate the cause of the contamination and verify that *E. coli* is negative by taking five samples over a 24-hour period from the same sampling site that originally tested positive for *E.*

coli. We expect that recordkeeping for the followup test for *E. coli* will also take about 5 minutes per test. As shown in table 1 of this document, we expect that three bottlers per year will test positive for *E. coli* in source water and will have to carry out the additional *E. coli* testing, with a burden of 1 hour. These bottlers will also have to keep records about rectifying the source contamination, for a burden of 2 hours. For all expected total coliform testing, *E. coli* testing, and source rectification, we estimate a total burden of 179 hours.

We base our estimate on our experience with the current CGMP regulations.

Dated: November 1, 2018.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2018-24322 Filed 11-6-18; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2018-D-3860]

Hypertension: Developing Fixed-Combination Drug Products for Treatment; Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a final guidance for industry entitled “Hypertension: Developing Fixed-Combination Drug Products for Treatment.” The purpose of this guidance is to assist sponsors in the clinical development of fixed-combination drug products for the treatment of hypertension. The guidance focuses on development of two-drug combinations of previously approved drug products. This guidance incorporates the comments received for and finalizes the draft guidance for industry entitled “Hypertension: Developing Fixed-Dose Combination Drugs for Treatment” issued on January 26, 2018.

DATES: The announcement of the guidance is published in the **Federal Register** on November 7, 2018.

ADDRESSES: You may submit either electronic or written comments on Agency guidances at any time as follows:

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-2018-D-3860 for “Hypertension: Developing Fixed-Combination Drug Products for Treatment.” Received comments 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.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

FOR FURTHER INFORMATION CONTACT:

Naomi Lowy, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave. Bldg. 22, Rm. 4204, Silver Spring, MD 20993-0002, 301-796-0692.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a guidance for industry entitled “Hypertension: Developing Fixed-Combination Drug Products for Treatment.” The purpose of this