

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2017-N-7012]

Agency Information Collection Activities; Proposed Collection; Comment Request; Use of Public Human Genetic Variant Databases To Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics

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 information collection associated with FDA recognition of public human genetic variant databases to support clinical validity for genetic and genomic-based in vitro diagnostics.

DATES: Submit either electronic or written comments on the collection of information by November 23, 2020.

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 November 23, 2020. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of November 23, 2020. 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-2017-N-7012 for "Agency Information Collection Activities; Proposed Collection; Comment Request; Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics." 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, 240-402-7500.

- **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.govinfo.gov/content/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, 240-402-7500.

FOR FURTHER INFORMATION CONTACT: Ila S. Mizrachi, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-7726, PRASStaff@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501-3521), 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.

Agency Information Collection Activities; Proposed Collection; Comment Request; Use of Public Human Genetic Variant Databases To Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics

OMB Control Number 0910-0850—Extension

Section 2011 of the 21st Century Cures Act of 2016 (Pub. L. 114-255) encourages the FDA to develop new approaches for addressing regulatory science issues as part of the Precision Medicine Initiative (PMI).

In the **Federal Register** of January 17, 2018 (83 FR 2451), FDA announced the availability of a guidance for industry

entitled “Use of Public Human Genetic Variant Databases To Support Clinical Validity for Next Generation Sequencing-Based In Vitro Diagnostics.” The guidance describes one part of FDA's PMI effort to create a flexible and adaptive regulatory approach to the oversight of next generation sequencing (NGS)-based tests. The goal of this effort is to help ensure patients receive accurate and meaningful test results, while promoting innovation in test development. The guidance describes how publicly accessible databases of human genetic variants can serve as sources of valid scientific evidence to support the clinical validity of genotype-phenotype relationships in FDA's regulatory review of both NGS-based tests and genetic and genomic tests based on other technologies. Publicly accessible genetic databases may be useful to support the clinical validity of NGS tests as well as single gene or panel tests that use other technology.

The guidance describes FDA's considerations in determining whether a genetic variant database is a source of valid scientific evidence that could support the clinical validity of an NGS-based test. The guidance further

outlines the process by which administrators¹ of genetic variant databases could voluntarily apply to FDA for recognition, and how FDA would review such applications and periodically reevaluate recognized databases. The guidance also recommends that, at the time of recognition, the database administrator make information regarding policies, procedures, and conflicts of interest publicly available and accessible on the genetic variant database's website.

Respondents are administrators of genetic databases. Our estimate of five respondents per year is based on the current number of databases that may meet FDA recommendations for recognition and seek such recognition.

Based on our experience and the nature of the information, we estimate that it will take an average of 80 hours to complete and submit an application for recognition. We estimate that maintenance of recognition activities will take approximately one-fourth of that time (20 hours) annually. We estimate that it will take approximately 1 hour to post the information on the website.

FDA estimates the burden of this collection of information as follows:

TABLE 1—ESTIMATED ANNUAL REPORTING BURDEN¹

| Activity | Number of respondents | Number of responses per respondent | Total annual responses | Average burden per response | Total hours |
|---|-----------------------|------------------------------------|------------------------|-----------------------------|-------------|
| Application for recognition of genetic database | 5 | 1 | 5 | 80 | 400 |

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

TABLE 2—ESTIMATED ANNUAL RECORDKEEPING BURDEN¹

| Activity | Number of recordkeepers | Number of records per recordkeeper | Total annual records | Average burden per recordkeeping | Total hours |
|---|-------------------------|------------------------------------|----------------------|----------------------------------|-------------|
| Maintenance of recognition activities | 5 | 1 | 5 | 20 | 100 |

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

TABLE 3—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN¹

| Activity | Number of respondents | Number of disclosures per respondent | Total annual disclosures | Average burden per disclosure | Total hours |
|--|-----------------------|--------------------------------------|--------------------------|-------------------------------|-------------|
| Public disclosure of policies, procedures, and conflicts of interest | 5 | 1 | 5 | 1 | 5 |

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

¹ FDA acknowledges that many databases may not use the term “administrator” or may have a

committee of individuals that oversee the database. Therefore, for the purpose of this guidance, a

genetic variant database administrator is the entity or entities that oversee database operations.

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

Dated: September 16, 2020.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2020-20960 Filed 9-22-20; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2020-N-1879]

Determination That PREXXARTAN (Valsartan) Oral Solution, 20 Milligrams/5 Milliliters and 80 Milligrams/20 Milliliters, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) has determined that PREXXARTAN (valsartan) oral solution, 20 milligrams (mg)/5 milliliters (mL) and 80 mg/20 mL, was not withdrawn from sale for reasons of safety or effectiveness. This determination will allow FDA to approve abbreviated new drug applications (ANDAs) for valsartan oral solution, 20 mg/5 mL and 80 mg/20 mL, if all other legal and regulatory requirements are met.

FOR FURTHER INFORMATION CONTACT: Robin Fastenau, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6236, Silver Spring, MD 20993-0002, 240-402-4510, robin.fastenau@fda.hhs.gov.

SUPPLEMENTARY INFORMATION: In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) (the 1984 amendments), which authorized the approval of duplicate versions of drug products under an ANDA procedure. ANDA applicants must, with certain exceptions, show that the drug for which they are seeking approval contains the same active ingredient in the same strength and dosage form as the “listed drug,” which is a version of the drug that was previously approved. ANDA applicants do not have to repeat the extensive

clinical testing otherwise necessary to gain approval of a new drug application (NDA).

The 1984 amendments include what is now section 505(j)(7) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)(7)), which requires FDA to publish a list of all approved drugs. FDA publishes this list as part of the “Approved Drug Products With Therapeutic Equivalence Evaluations,” which is known generally as the “Orange Book.” Under FDA regulations, drugs are removed from the list if the Agency withdraws or suspends approval of the drug’s NDA or ANDA for reasons of safety or effectiveness or if FDA determines that the listed drug was withdrawn from sale for reasons of safety or effectiveness (§ 314.162 (21 CFR 314.162)).

A person may petition the Agency to determine, or the Agency may determine on its own initiative, whether a listed drug was withdrawn from sale for reasons of safety or effectiveness. This determination may be made at any time after the drug has been withdrawn from sale, but must be made prior to approving an ANDA that refers to the listed drug (§ 314.161 (21 CFR 314.161)). FDA may not approve an ANDA that does not refer to a listed drug.

PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, is the subject of NDA 209139, held by Carmel Biosciences, Inc., and initially approved on December 19, 2017. PREXXARTAN is indicated for hypertension in adults and children 6 years and older, to lower blood pressure; for heart failure by significantly reducing hospitalization for patients who are unable to swallow valsartan tablets; and for stable left ventricular failure or left ventricular dysfunction following myocardial infarction.

PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, is currently listed in the “Discontinued Drug Product List” section of the Orange Book. Additionally, Carmel Biosciences has never marketed PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL. In previous instances (see, e.g., 72 FR 9763, March 5, 2007; 61 FR 25497, May 21, 1996), the Agency has determined that, for purposes of §§ 314.161 and 314.162, never marketing an approved drug product is equivalent to withdrawing the drug from sale.

Novitium Pharma LLC submitted a citizen petition dated January 30, 2020

(Docket No. FDA-2020-P-0511), under 21 CFR 10.30, requesting that the Agency determine whether PREXXARTAN (valsartan) oral solution, 20 mg/5 mL, was withdrawn from sale for reasons of safety or effectiveness. Although the citizen petition did not address the 80 mg/20 mL strength, that strength has also been discontinued. On our own initiative, we have also determined whether that strength was withdrawn for safety or effectiveness reasons.

After considering the citizen petition and reviewing Agency records and based on the information we have at this time, FDA has determined under § 314.161 that PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, was not withdrawn for reasons of safety or effectiveness. The petitioner has identified no data or other information suggesting that this drug product was withdrawn for reasons of safety or effectiveness. We have carefully reviewed our files for records concerning the withdrawal of PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, from sale. We have also independently evaluated relevant literature and data for possible postmarketing adverse events. We have reviewed the available evidence and determined that this drug product was not withdrawn from sale for reasons of safety or effectiveness.

Accordingly, the Agency will continue to list PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, in the “Discontinued Drug Product List” section of the Orange Book. The “Discontinued Drug Product List” delineates, among other items, drug products that have been discontinued from marketing for reasons other than safety or effectiveness. ANDAs that refer to PREXXARTAN (valsartan) oral solution, 20 mg/5 mL and 80 mg/20 mL, may be approved by the Agency as long as they meet all other legal and regulatory requirements for the approval of ANDAs. If FDA determines that labeling for this drug product should be revised to meet current standards, the Agency will advise ANDA applicants to submit such labeling.

Dated: September 17, 2020.

Lauren K. Roth,

Associate Commissioner for Policy.

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