



4164-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2019-D-1876]

### Testing for Biotin Interference in In Vitro Diagnostic Devices; 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 entitled "Testing for Biotin Interference in In Vitro Diagnostic Devices; Guidance for Industry." The guidance provides FDA's recommendations on the testing for interference by biotin on the performance of in vitro diagnostic devices (IVDs). The guidance is intended to help device developers and clinicians understand how FDA recommends biotin interference testing be performed, and how the results of the testing should be communicated to end users, including clinical laboratories and clinicians. The guidance announced in this notice finalizes the draft guidance of the same title dated June 2019.

**DATES:** The announcement of the guidance is published in the *Federal Register* on [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].

**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-2019-D-1876 for "Testing for Biotin Interference in In Vitro Diagnostic Devices; Guidance for Industry."

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, 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.

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

Submit written requests for single copies of the guidance to the Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002 or the Office of Policy, Guidance and Policy Development, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 5431, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist the office in processing your requests. The guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 240-402-8010. See the SUPPLEMENTARY INFORMATION section for electronic access to the guidance document.

**FOR FURTHER INFORMATION CONTACT:** Shruti Modi, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

**SUPPLEMENTARY INFORMATION:**

I. Background

FDA is announcing the availability of a document entitled "Testing for Biotin Interference in In Vitro Diagnostic Devices; Guidance for Industry." The guidance provides FDA's recommendations on the testing for interference by biotin on the performance of IVDs. The guidance is intended to help device developers and clinicians understand how FDA recommends biotin interference testing be performed, and how the results of the testing should be communicated to end users, including clinical laboratories and clinicians. The

recommendations apply to IVDs, including devices that are licensed under section 351 of the Public Health Service Act (42 U.S.C. 262) and used in donor screening, that use biotin technology.

Biotin, also known as vitamin B7, is a water-soluble vitamin often found in multivitamins, prenatal vitamins, and dietary supplements marketed for hair, skin, and nail growth. FDA has become aware of potential biotin interference with IVDs that use biotin/avidin interactions as part of the device technology. Biotin levels in samples from patients who consume more than the recommended daily intake of biotin can cause falsely high or falsely low results, depending on the test principle.

In the *Federal Register* of June 10, 2019 (84 FR 27781), FDA announced the availability of the draft guidance of the same title. FDA received a few comments on the draft guidance and those comments were considered as the guidance was finalized. We considered comments on the recommended level of biotin concentration for evaluation. We decline to recommend evaluating a concentration level below 3,500 nanograms per milliliter. We believe this level is appropriate for minimizing the risk to patients from incorrect test results. Further, this level is consistent with best practices among the industry to test at three times the highest concentration levels observed, as recommended in the FDA-recognized standard published by the Clinical Laboratory Standards Institute. Other comments recommended FDA clarify or expand upon the necessity of mitigation strategies to address biotin interference other than labeling. We decline to recommend other specific mitigation strategies, but note that other mitigation strategies such as customer information letters and technical mitigations may be considered when the risk of potentially incorrect results from biotin interference could significantly affect patient or public health. Finally, we considered comments regarding additional types of information to be

communicated to end-users, but we declined to provide more specific recommendations because manufacturers may not have sufficient data to provide more specific information in the labeling. In addition, editorial edits were made to improve clarity. The guidance announced in this notice finalizes the draft guidance of the same title dated June 2019.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on testing for biotin interference in in vitro diagnostic devices. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

## II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR part 809 have been approved under OMB control number 0910-0485.

## III. Electronic Access

Persons with access to the internet may obtain the guidance at either <https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products>, or <https://www.regulations.gov>.

Dated: October 9, 2020.

**Lauren K. Roth,**

*Acting Principal Associate Commissioner for Policy.*

[FR Doc. 2020-22926 Filed: 10/15/2020 8:45 am; Publication Date: 10/16/2020]