TABLE 3—ESTIMATED ANNUAL THIRD-PARTY DISCLOSURE BURDEN [1]

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.

This draft guidance also refers to previously approved collections of information. These collections of information are subject to review by the OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in the guidance document ''Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff'' have been approved under OMB control number 0910–0756. The collections of information regarding premarket submissions have been approved as follows: The collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910–0120; and the collections of information in 21 CFR part 814, subparts A through E, have been approved under OMB control number 0910–0231.

V. Other Issues for Consideration

The Agency invites comments on the draft guidance document entitled ''Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics,'' in general, and on the following questions, in particular:

1. Should the quality recommendations outlined in the guidance apply equally to databases of somatic variants and to germline variants?

2. While this document applies to NGS-based tests, FDA expects that it may also be relevant to genetic tests that use other technologies (*e.g.,* polymerase chain reaction, Sanger sequencing, etc.). Are any additional considerations necessary to support the use of these databases in the premarket review of tests using technologies other than NGS, should FDA decide to apply this approach more broadly in the future?

3. FDA recognizes that the evidence linking specific variants to diseases or conditions will change over time, and as such, assertions about those variants may also change. If an assertion regarding a variant changes over time, how should FDA assess what regulatory actions may be appropriate with respect to in IVDs supported by such assertions? How often should FDA conduct ongoing review of an FDA-recognized database?

4. FDA notes that databases may have ''discordant calls'' with other databases, where the assertions for a variant in each database vary. While FDA believes that these discordant calls often arise because one database has information the other does not and our proposed policy will mitigate these issues over time; what, if any, action should FDA take when it learns about discordant calls between two databases with respect to database recognition or IVDs supported by such calls in FDA-recognized databases?

5. FDA has requested information regarding conflicts of interest for curators and personnel of databases seeking FDA recognition. FDA acknowledges that many personnel involved with variant curation and interpretation may have some connection to NGS test developers. What type of information should FDA collect and what policies should it implement to mitigate such potential conflicts of interest in FDA-recognized databases?

Dated: July 5, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016–16200 Filed 7–7–16; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2016–D–1270]

Use of Standards in the Food and Drug Administration's Regulatory Oversight of Next Generation Sequencing-Based In Vitro Diagnostics Used for Diagnosing Germline Diseases; Draft Guidance for Stakeholders and Food and Drug Administration Staff; 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 the draft guidance entitled ''Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases.'' As part of the White House's Precision Medicine Initiative (PMI),[1] FDA is issuing this draft guidance to provide FDA's proposed approach on the content and possible use of standards in providing oversight for targeted and whole exome human DNA sequencing (WES) NGS-based tests intended to aid in the diagnosis of individuals with suspected germline diseases or other conditions. This document provides recommendations for designing, developing, and validating NGS-based tests for germline diseases, and also discusses possible use of FDA-recognized standards for regulatory oversight of these tests. These recommendations are based on FDA's understanding of the tools and processes needed to run an NGS-based test along with the design and analytical validation considerations appropriate for such tests. This draft guidance is not final nor is it in effect at this time.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment of this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by October 6, 2016.

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

[1] The Precision Medicine Initiative found on the White House's Web site at: *https://www.whitehouse.gov/precision-medicine.*

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–2016–D–1270 for ''Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases.'' 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.

An electronic copy of the guidance document is available for download from the Internet. See the **SUPPLEMENTARY INFORMATION** section for information on electronic access to the guidance. Submit written requests for a single hard copy of the draft guidance document entitled ''Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases'' to the Office of the Center Director, 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; or the Office of Communication, Outreach, and Development, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your request.

FOR FURTHER INFORMATION CONTACT: Personalized Medicine Staff, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4544, Silver Spring, MD 20993–0002, 301–796–6206; or *PMI@fda.hhs.gov;* or Stephen Ripley, 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

As part of the PMI, FDA is committed to implementing a flexible and adaptive regulatory oversight approach, which fosters innovation and simultaneously assures that patients have access to accurate and meaningful test results. FDA held two public workshops on this issue: ''Optimizing FDA's Regulatory Oversight of Next Generation Sequencing Diagnostic Tests Public Workshop'' held on February 20, 2015, and ''Standards Based Approach to Analytical Performance Evaluation of Next Generation Sequencing In Vitro Diagnostic Tests'' held on November 12, 2016. This guidance document, when finalized, provides recommendations for designing, developing, and validating for targeted and whole exome human DNA sequencing (WES) NGS-based tests intended to aid in the diagnosis of individuals with suspected germline diseases or other conditions (hereinafter referred to as ''NGS-based tests for germline diseases'' or ''NGS-based tests''). It also outlines considerations for possibly classifying certain NGS-based tests for germline diseases in class II and exempting them from premarket notification requirements. Upon finalization of this guidance, these recommendations should be used as guidelines for test developers for premarket submissions. However, the longer-term goal is for these recommendations to form the basis for standards that FDA could recognize or for special controls and/or conditions for premarket notification (510(k)) exemption. FDA is also issuing a draft guidance entitled ''Use of Public Human Genetic Variant Databases to Support Clinical Validity for Next Generation Sequencing (NGS)-Based In Vitro Diagnostics'' which is being issued concurrently elsewhere in this issue of the **Federal Register**.

II. Significance of Guidance

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on use of standards in FDA regulatory oversight of NGS-based IVDs used for diagnosing germline diseases. 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.

III. Electronic Access

Persons interested in obtaining a copy of the draft guidance may do so by downloading an electronic copy from the Internet. A search capability for all Center for Devices and Radiological Health guidance documents is available at *http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm,* and for Center for Biologics Evaluation and Research guidance documents is available at *http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.* Guidance documents are also available at *http://www.regulations.gov.* Persons unable to download an electronic copy of ''Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases'' may send an email request to *CDRH-Guidance@fda.hhs.gov* to receive an electronic copy of the document. Please use the document number 16009 to identify the guidance you are requesting.

IV. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). The collections of information in 21 CFR part 807, subpart E, regarding premarket notification submissions, have been approved under OMB control number 0910–0120; the collections of information in 21 CFR part 801 and 21 CFR 809.10, regarding labeling, have been approved under OMB control number 0910–0485; the collections of information in 21 CFR part 814, subparts A through E, regarding premarket approval, have been approved under OMB control number 0910–0231; the collections of information in 21 CFR part 820, regarding the quality system regulation, have been approved under OMB control number 0910–0073; and the collections of information in the guidance document ''Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff'' have been approved under OMB control number 0910–0756.

V. Other Issues for Consideration

The Agency invites comments on the draft guidance document entitled ''Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases,'' in general, and on the following questions, in particular:

1. Does the draft guidance content adequately address the analytical performance of targeted and whole exome human DNA sequencing (WES) NGS-based tests intended to aid in the diagnosis of individuals with suspected germline diseases or other conditions (referred to as ''NGS-based tests for germline diseases'' or ''NGS-based tests'' in the guidance)? For example, do the recommendations outlined in the draft guidance adequately address the analytical performance of NGS-based tests used as an aid in diagnosis of patients with signs and symptoms of developmental delay or intellectual disability, undiagnosed diseases, or hereditary cancer syndromes? If not, what additional test design, development, or validation activities are necessary for analytical validation of such tests? Are there specific indications within this broad intended use that require different or additional test design, development, or validation activities from those described in the draft guidance?

2. Do the recommendations in the draft guidance adequately address the analytical validation of NGS-based tests that use targeted panels or WES? Targeted sequencing panels? Are there differences between the use of targeted panels and WES that were not adequately distinguished in the recommendations described in the draft guidance?

3. The recommendations in this document focus on WES and targeted NGS-based tests for germline diseases. Are the recommendations outlined in the guidance sufficient to address analytical validation for whole genome sequencing (WGS) NGS-based tests for germline diseases? If not, what additional test design, development, and validation activities are needed to address the analytical validation of such tests?

4. Accuracy is generally described using an agreement, typically positive and negative percent agreement (PPA and NPA), between a new test and an accepted reference method. For NGS-based tests, positive predictive value (PPV) may be a more meaningful metric than NPA when calculating the likelihood that a variant call detected by the test is a true positive. If PPV is calculated using only analytical results without taking into account prevalence in a population, it is sometimes called ''technical'' PPV (TPPV) to distinguish it from prevalence-based PPV. What are the benefits and weaknesses to assessing NGS-based test accuracy using TPPV in addition to PPA and NPA, or instead of NPA?

5. Are the minimum performance thresholds presented in this draft guidance appropriate, or are alternative thresholds more appropriate? Are there ''best ways'' to determine acceptable thresholds for each metric? Are there performance metrics that do not require minimum thresholds? Are there test scenarios where minimum thresholds are not useful or relevant?

6. How can bias and over-fitting be minimized or accounted for if known ''reference'' samples are used as comparators in accuracy studies?

Dated: July 5, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016–16201 Filed 7–7–16; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–1206]

Authorization of Emergency Use of an In Vitro Diagnostic Device for Detection of Ebola Zaire Virus; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of an Emergency Use Authorization (EUA) (the Authorization) for an in vitro diagnostic device for detection of the Ebola Zaire virus in response to the Ebola virus outbreak in West Africa. FDA issued this Authorization under the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as requested by Biocartis NV. The Authorization contains, among other things, conditions on the emergency use of the authorized in vitro diagnostic device. The Authorization follows the September 22, 2006, determination by then-Secretary of the Department of Homeland Security (DHS), Michael Chertoff, that the Ebola virus presents a material threat against the U.S. population sufficient to affect national security. On the basis of such determination, the Secretary of Health