Proposed Rules

Federal Register
Vol. 86, No. 224
Wednesday, November 24, 2021

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 866

[Docket No. FDA–2020–N–2297]

Microbiology Devices; Reclassification of Human Immunodeficiency Virus Viral Load Monitoring Tests

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed amendment; proposed order.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is proposing to reclassify human immunodeficiency virus (HIV) viral load monitoring tests, a postamendments class III device with the product code MZF, into class II (special controls), subject to premarket notification. FDA is also proposing a new device classification regulation along with special controls that the Agency believes are necessary to provide a reasonable assurance of safety and effectiveness for this device type. FDA is proposing this reclassification on its own initiative. If finalized, this order will reclassify this device type from class III (premarket approval) to class II (special controls) and reduce the regulatory burdens associated with these devices because manufacturers will no longer be required to submit a premarket approval application (PMA) for this device type but can instead submit a less burdensome premarket notification (510(k)) and receive clearance before marketing their device.

DATES: Submit either electronic or written comments on the proposed order by January 24, 2022. See section XI of this document for the proposed effective date of any final order based on this proposed order.

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 24, 2022. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of January 24, 2022. 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–2020–N–2297 for ''Microbiology Devices; Reclassification of Human Immunodeficiency Virus Viral Load Monitoring Tests.'' 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: Myrna Hanna, Center for Biologics Evaluation and Review, Food and Drug Administration, 10903 New Hampshire

Ave., Bldg. 66, Rm. 5513, Silver Spring, MD 20993–0002, 301–796–5739.

SUPPLEMENTARY INFORMATION:

I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Pub. L. 94–295), the Safe Medical Devices Act of 1990 (Pub. L. 101–629), the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105–115), the Medical Device User Fee and Modernization Act of 2002 (Pub. L. 107–250), the Medical Devices Technical Corrections Act (Pub. L. 108–214), the Food and Drug Administration Amendments Act of 2007 (Pub. L. 110–85), and the Food and Drug Administration Safety and Innovation Act (Pub. L. 112–144), among other amendments, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (general controls and special controls), and class III (general controls and premarket approval).

Section 513(a)(1) of the FD&C Act defines the three classes of devices. Class I devices are those devices for which the general controls of the FD&C Act (controls authorized by or under sections 501, 502, 510, 516, 518, 519, or 520 (21 U.S.C. 351, 352, 360, 360f, 360h, 360i, or 360j) or any combination of such sections) are sufficient to provide reasonable assurance of safety and effectiveness; or those devices for which insufficient information exists to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness or to establish special controls to provide such assurance, but because the devices are not purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, and do not present a potential unreasonable risk of illness or injury, are to be regulated by general controls (section 513(a)(1)(A) of the FD&C Act). Class II devices are those devices for which general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness and for which there is sufficient information to establish special controls to provide such assurance, including the promulgation of performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and other appropriate actions the Agency deems necessary to provide such assurance (section 513(a)(1)(B) of the FD&C Act). Class III devices are those devices for which insufficient information exists to determine that general controls and special controls would provide a reasonable assurance of safety and effectiveness, and are purported or represented to be for a use in supporting or sustaining human life or for a use which is of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury (section 513(a)(1)(C) of the FD&C Act).

Devices that were not in commercial distribution prior to May 28, 1976 (generally referred to as postamendments devices) are automatically classified by section 513(f)(1) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval unless, and until, (1) FDA reclassifies the device into class I or class II, or (2) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. FDA determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the FD&C Act and part 807 (21 CFR part 807), subpart E, of the regulations.

A postamendments device that has been initially classified in class III under section 513(f)(1) of the FD&C Act may be reclassified into class I or II under section 513(f)(3) of the FD&C Act. Section 513(f)(3) of the FD&C Act provides that FDA, acting by administrative order, can reclassify the device into class I or class II on its own initiative, or in response to a petition from the manufacturer or importer of the device. To change the classification of the device, the proposed new class must have sufficient regulatory controls to provide a reasonable assurance of the safety and effectiveness of the device for its intended use.

FDA relies upon ''valid scientific evidence,'' as defined in section 513(a)(3) and 21 CFR 860.7(c)(2), in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the ''valid scientific evidence'' upon which the Agency relies must be publicly available (see section 520(c) of the FD&C Act). Publicly available information excludes trade secret and/or confidential commercial information, *e.g.,* the contents of a pending PMA (see section 520(c) of the FD&C Act).

In accordance with section 513(f)(3) of the FD&C Act, the Agency is proposing to reclassify HIV viral load monitoring tests, a postamendments class III device, into class II (special controls), subject to premarket notification because the Agency believes the standard in 513(a)(1)(B) of the FD&C Act is met because there is sufficient information to establish special controls, which, in addition to general controls, will provide reasonable assurance of the safety and effectiveness of the device.[1]

Section 510(m) of the FD&C Act provides that a class II device may be exempted from the 510(k) premarket notification requirements under section 510(k) of the FD&C Act if the Agency determines that premarket notification is not necessary to reasonably assure the safety and effectiveness of the device. FDA has determined that premarket notification is necessary to reasonably assure the safety and effectiveness of HIV viral load monitoring tests. Therefore, the Agency does not intend to exempt this proposed class II device from premarket notification (510(k)) submission under section 510(m) of the FD&C Act.

II. Regulatory History of the Devices

This proposed order addresses HIV viral load monitoring tests. These are prescription tests that measure HIV RNA as an aid in monitoring patient status and are assigned product code MZF.[2] These postamendments devices are currently regulated as class III devices under section 513(f)(1) of the FD&C Act. Based on our review experience and consistent with the FD&C Act and FDA's regulations in 21 CFR 860.134, FDA believes that these devices should be reclassified from class III into class II with special controls because special controls, in addition to general controls, are necessary and sufficient to provide reasonable assurance of the safety and effectiveness of these devices and there is sufficient

[1] In December 2019, FDA began adding the term ''Proposed amendment'' to the ''ACTION'' caption for these documents, typically styled ''Proposed order'', to indicate that they ''propose to amend'' the Code of Federal Regulations. This editorial change was made in accordance with the Office of Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

[2] On February 21, 2020, FDA published a separate proposed order to reclassify certain HIV serological diagnostic and supplemental tests and HIV nucleic acid diagnostic and supplemental tests, which are also currently assigned product code MZF, from class III into class II (85 FR 10110).

information to establish special controls to provide such assurance.

FDA approved the first in vitro nucleic acid amplification-based HIV viral load test on June 3, 1996, for the quantitation of HIV–1 RNA in human plasma. Currently, there are six HIV viral load monitoring tests on the market, all of which met the performance criteria specified in the proposed special controls, considered necessary for the intended use of the test, when they were approved by FDA (Ref. 1).

A review of the FDA's medical device reporting database, MAUDE (Manufacturer and User Facility Device Experience), indicates a low number of reported events for HIV viral load monitoring tests. Millions of devices intended for use as HIV viral load monitoring tests have been sold since 1996 with fewer than 200 reported adverse events as of October 2020. Of these events, fewer than 10 are reported to involve injuries due to incorrect results; the remainder are malfunctions, such as user errors or incorrect results, that had no reported effect on the individual being monitored. There has been one class II recall and no class I (highest risk) recalls specific to HIV viral load monitoring tests, which, coupled with the low number of reported events, indicates a good safety record for this device class.

III. Device Description

This proposed order applies to HIV viral load monitoring tests that are prescription in vitro diagnostic devices for monitoring of HIV viral load in body fluids. As such, these prescription devices must satisfy prescription labeling requirements for in vitro diagnostic products (see 21 CFR 809.10(a)(4) and (b)(5)(ii)). HIV viral load monitoring tests are intended for use in the clinical management of individuals living with HIV and are for professional use only. These devices are not intended for use as an aid in diagnosis or for screening donors of blood or blood products or human cells, tissues, or cellular and tissue-based products (HCT/Ps).

HIV viral load monitoring tests are quantitative in vitro diagnostic tests that measure the amount of HIV RNA in human body fluids such as plasma and whole blood. The HIV RNA is isolated, amplified, and detected by labeled probes that produce a quantitative output that determines the amount of HIV in the sample. The test results then are used as part of patient management decisions in conjunction with other relevant clinical and laboratory findings.

Approval of HIV viral load monitoring tests has been based on studies and established clinical decision points that demonstrate that changes in viral load correlate with clinically meaningful outcomes, meaning that HIV RNA measurements could reliably assess the success or failure of antiretroviral therapy (ART) (Ref. 1).

IV. Proposed Reclassification

FDA is proposing to reclassify HIV viral load monitoring tests. At a public meeting held on July 19, 2018, the Blood Products Advisory Committee, convened as a medical device panel (''the Panel''), unanimously agreed that special controls, in addition to general controls, are sufficient to mitigate the risk to health from incorrect results from HIV nucleic acid and serological diagnostic and supplemental tests. The Panel believed that class II with the special controls would provide reasonable assurance of the safety and effectiveness of those devices. In February 2020, FDA issued a proposed order that, if finalized, would reclassify those devices from class III into class II (85 FR 10110). As part of the Panel's discussion, the Panel also recommended that FDA consider reclassification of quantitative HIV tests indicated for use for monitoring HIV viral load from class III to class II (Ref. 2).

In accordance with section 513(f)(3) of the FD&C Act and 21 CFR part 860, subpart C, FDA is proposing to reclassify postamendments HIV viral load monitoring tests from class III into class II. FDA believes that there are sufficient data and information available through FDA's accumulated experience with these devices and from published literature to demonstrate that the proposed special controls, along with general controls, would effectively mitigate the risks to health identified in section V of this document and provide reasonable assurance of safety and effectiveness of these devices. Absent the special controls identified in this proposed order, general controls applicable to the device are insufficient to provide reasonable assurance of the safety and effectiveness.

FDA is proposing to create a separate classification regulation for HIV viral load monitoring tests. Under this proposed order, if finalized, HIV viral load monitoring tests will be reclassified from class III to class II and identified as prescription devices. In this proposed order the Agency has proposed the special controls under section 513(a)(1)(B) of the FD&C Act that, together with general controls, would provide reasonable assurance of the safety and effectiveness of HIV viral load monitoring tests.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. For these HIV viral load monitoring tests, FDA has determined that premarket notification is necessary to provide a reasonable assurance of safety and effectiveness. Therefore, FDA does not intend to exempt this proposed class II device from the 510(k) requirements. If this proposed order is finalized, persons who intend to market this type of device must submit to FDA a 510(k) and receive clearance prior to marketing the device.

This proposed order, if finalized, will decrease regulatory burden on industry because manufacturers will no longer have to submit a PMA for this device type, but can instead submit a 510(k) to the Agency for review prior to marketing their device. A 510(k) is a less-burdensome pathway to market a device, which typically results in a shorter premarket review timeline compared with a PMA, helping to provide more timely access to this device type to patients. FDA expects that the reclassification of these devices would enable more manufacturers to develop HIV viral load monitoring tests such that patients would benefit from increased access to safe and effective tests.

V. Risks to Health

Viral load is one of the important markers for monitoring the effectiveness of ART and disease progression. The Department of Health and Human Services (HHS) in 2014 issued guidelines on the treatment of HIV in adults and adolescents in United States. The guidelines are updated periodically based on new data. Regarding viral load monitoring, the HHS guidelines define optimal viral load suppression as suppressing viral load levels persistently to <20 to 75 copies per milliliter (/mL) of HIV RNA, depending on the assay used (Ref. 3). Virologic failure, at which point changes in treatment are considered, is defined as the inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 copies/mL (Ref. 3). The HHS guidelines recommend that viral load testing should be performed for all patients with HIV at entry into care, initiation of therapy, and on a regular basis thereafter (Ref. 3). Therefore, improving access to HIV viral

load monitoring tests is a public health priority. After considering FDA's accumulated experience with these devices from review submissions and the published literature, FDA has identified the following probable risks to health associated with HIV viral load monitoring tests:

(1) An inaccurately low viral load test result may influence patient management decisions, such as continuation of ineffective treatment, which can lead to serious injury including death. Inaccurately low viral load test results also may contribute to public health risk by leading to inadvertent transmission of the virus by an individual living with HIV. Factors that may cause decreased test sensitivity and/or increased risk of inaccurately low viral load test results include, but are not limited to, viral strain variability, acquisition of de novo mutations in genomic regions of HIV targeted by the device, and the presence of interfering substances in the sample. Inaccurately low results also can be caused by improper sample collection or sample handling, loss of sensitivity of the device, failure of detection reagents, and failure of instruments.

(2) An inaccurately high viral load test result may contribute to an unnecessary change in therapy, potentially ending effective treatment and leading to less effective management of disease, as well as significant emotional stress. Factors that may cause an increased rate of inaccurately high viral load test results include, but are not limited to, cross-reactivity with other substances in the sample, carryover, viral strain variability, or acquisition of de novo mutations in genes other than HIV. Inaccurately high results also can be caused by improper sample collection and sample contamination.

(3) Incorrect interpretation of test results by healthcare professionals may result in patient management decisions, such as continuation of ineffective therapy or an unnecessary change in therapy, that could lead to serious injury, including death, and less effective management of the disease. Incorrect interpretation of results may be caused by inadequate labeling, including insufficient limitations, warnings, and explanations of test procedure.

VI. Summary of the Reasons for Reclassification

FDA believes that HIV viral load monitoring tests should be reclassified from class III into class II (special controls) because special controls, in addition to general controls, can be established to mitigate the risks to health identified in section V and provide reasonable assurance of the safety and effectiveness of this device type. The proposed special controls are identified by FDA in section VII of this proposed order. FDA's reasons for reclassification are as follows:

(1) There is substantial scientific and medical information available regarding the nature and complexity of, and risks associated with, HIV viral load monitoring tests (Refs. 3 to 11). The safety and effectiveness of this device type has become well-established by the performance of the approved HIV viral load tests (Ref. 1).

(2) Risks associated with the failure of the device to perform as indicated (*e.g.,* inaccurately high or low test results) and risks associated with incorrect interpretation of results can be mitigated through a combination of special controls, including performance criteria, certain labeling requirements, and submission of certain manufacturing information. Performance criteria would consist primarily of analytical and method comparison study design specifications and acceptance criteria that are based on public information regarding the performance and validation of previously approved devices. FDA expects that a device would demonstrate acceptable performance, *e.g.,* analytical sensitivity, at clinically relevant medical decision points at the time of clearance. This would help ensure that devices meet or exceed the performance of other cleared or approved HIV viral load tests at existing clinically relevant medical decision points and, in the future, demonstrate similar performance if there are changes in those medical decision points that reflect additional evidence and/or medical advances. Examples of labeling mitigations include appropriate limitations, including that results should be interpreted in conjunction with the individual's clinical presentation, history, and other laboratory results. These are necessary to ensure that the devices are used correctly, and the results are interpreted appropriately, given the diversity of settings in which these devices are intended to be used. Manufacturing information required to be submitted would include summaries of strategies to quantitate new HIV types, subtypes, genotypes, and mutations to ensure the tests continue to monitor clinically relevant forms of HIV. It also would include a detailed device description, including information on number and design of primers and probes, which should be designed according to current best practices and professional recommendations. It would also include appropriate and acceptable procedures to determine the severity of events to ensure appropriate adverse event reporting, protocols for assessing stability, and evaluation of test performance at the extremes of specifications to ensure the tests have been validated to function correctly under diverse conditions.

Taking into account the established health benefits of the use of the device and the nature of the probable risks of the device (Refs. 1, 3 to 11), FDA, on its own initiative, is proposing to reclassify these postamendments devices from class III into class II. FDA believes that, when used as indicated, HIV viral load monitoring tests can provide significant benefits to clinicians and patients.

VII. Proposed Special Controls

FDA believes that these devices can be classified into class II with the establishment of special controls. FDA believes that these special controls, in addition to general controls, will provide a reasonable assurance of the safety and efficacy of these devices. Table 1 demonstrates how these proposed special controls will mitigate each of the identified risks to health in section V.

TABLE 1—RISKS TO HEALTH AND MITIGATION MEASURES FOR HIV VIRAL LOAD MONITORING TESTS

Identified risks to health	Mitigation measures
An inaccurately low test result may influence patient management decisions, including continuation of ineffective antiviral therapy which can lead to serious injury including death. An inaccurately low test result may contribute to public health risk by leading to inadvertent transmission of the virus by a person living with HIV.	Certain labeling limitations, warnings, and explanations of the procedures and interpretation results. Analytical sensitivity and method comparison study performance criteria. Acceptable strategies for monitoring emergence of and ability of the test to detect new or altered circulating forms of HIV. Certain other device verification and validation information, including acceptable processes for risk analysis, testing performance at extremes of specifications, and determining severity of adverse events and malfunctions.
An inaccurately high test result may contribute to unnecessary change in therapy, potentially disrupting effective treatment and leading to less effective management of disease, as well as significant emotional stress.	Labeling instructions for appropriate confirmation of elevated results. Analytical performance criteria. Acceptable validation of susceptibility to interference and cross-reactivity. Acceptable processes for risk analysis, testing performance at extremes of specifications, and determining severity of adverse events and malfunctions.
Incorrect interpretation of test results may result in patient management decisions, such as continuation of ineffective therapy or an unnecessary change in therapy, that could lead to serious injury, including death, and less effective management of the disease.	Certain labeling limitations, warnings, and explanations of the procedures and interpretation results.

If this proposed order is finalized, HIV viral load monitoring tests will be reclassified into class II (special controls). As discussed below, the reclassification will be codified in 21 CFR 866.3958. Firms submitting a 510(k) for an HIV viral load monitoring test will be required to comply with the particular mitigation measures set forth in the special controls. Adherence to the special controls, in addition to the general controls, is necessary to provide a reasonable assurance of the safety and effectiveness of the devices.

VIII. Analysis of Environmental Impact

The Agency has determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

FDA tentatively concludes that this proposed order contains no new collection 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. This proposed order refers to previously approved FDA collections of information. These collections of information are subject to review by the OMB under the PRA. The collections of information in 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 820 have been approved under OMB control number 0910–0073; the collections of information in 21 CFR part 803 have been approved under OMB control number 0910–0437; and the collections of information in 21 CFR parts 801 and 809 have been approved under OMB control number 0910–0485.

X. Codification of Orders

Under section 513(f)(3) of the FD&C Act, FDA may issue final orders to reclassify devices. FDA will continue to codify classifications and reclassifications in the Code of Federal Regulations (CFR). Changes resulting from final orders will appear in the CFR as newly codified orders. Therefore, under section 513(f)(3), in the proposed order, we are proposing to codify HIV viral load monitoring tests in the new 21 CFR 866.3958, under which HIV viral load monitoring tests would be reclassified from class III to class II.

XI. Proposed Effective Date

FDA proposes that any final order based on this proposed order become effective 30 days after its date of publication in the **Federal Register**.

XII. References

The following references are on display at the Dockets Management Staff (see **ADDRESSES**) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at *https://www.regulations.gov*. FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

1. List of approved HIV viral load monitoring tests with supporting information can be found at *https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/premarket-approvals-and-humanitarian-device-exemptions-supporting-documents.*
2. ''Reclassification of HIV Point of Care and Laboratory-based serological and NAT diagnostic devices from Class III (PMA) to Class II 510(k); Issue Summary Prepared for the July 19, 2018, Meeting of the Blood Products Advisory Committee (BPAC)).'' Available at: *https://www.fda.gov/advisory-committees/blood-products-advisory-committee/2018-meeting-materials-blood-products-advisory-committee.*
3. ''Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV.'' Department of Health and Human Services. Accessed November 24, 2020. Available at: *https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/antiretroviral-therapy-prevent-sexual-transmission-hiv.*
4. ''Human Immunodeficiency Virus-1 Infection: Developing Antiretroviral Drugs for Treatment; Guidance for Industry.'' Available at: *https://www.fda.gov/media/86284/download.*
5. Aberg, J.A., J.E. Gallant, K.H. Ghanem, et al., ''Primary Care Guidelines for the Management of Persons Infected with HIV: 2013 Update by the HIV Medicine Association of the Infectious Diseases Society of America,'' *Clinical Infectious Disease,* 58:e1–34, 2014.
6. Saag, M.S., M. Holodniy, D.R. Kuritzkes, et al., ''HIV Viral Load Markers in Clinical Practice,'' *Nature Medicine,* 2:625–629, 1996.
7. Das, M., P.L. Chu, G-M. Santos, et al., ''Decreases in Community Viral Load are Accompanied by Reductions in New HIV Infections in San Francisco,'' *PLoS ONE,* 5:e11068, 2010.
8. Stadhouders, R., S.D. Pas, J. Anber, et al., ''The Effect of Primer-Template Mismatches on the Detection and Quantification of Nucleic Acids Using the 5' Nuclease Assay,'' *Journal of Molecular Diagnostics,* 12:109–117, 2010.
9. Swenson, L.C., B. Cobb, A.M. Geretti, et al., ''Comparative Performances of HIV–

1 RNA Load Assays at Low Viral Load Levels: Results of an International Collaboration,'' *Journal of Clinical Microbiology,* 52(2):517–523, 2014.
10. Caniglia, E.C., C. Sabin, J.M. Robins, et al., ''When to Monitor CD4 Cell Count and HIV RNA to Reduce Mortality and AIDS-Defining Illness in Virologically Suppressed HIV-Positive Persons on Antiretroviral Therapy in High-Income Countries: A Prospective Observational Study,'' *Journal of Acquired Immune Deficiency Syndromes,* 72:214–221, 2016.
11. Shoko, C. and D. Chikobvu, ''A Superiority of Viral Load Over CD4 Cell Count When Predicting Mortality in HIV Patients on Therapy.'' *BioMed Central Infectious Diseases,* 19:169, 2019.

List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act it is proposed that 21 CFR part 866 be amended as follows:

PART 866—IMMUNOLOGY AND MICROBIOLOGY DEVICES

■ 1. The authority citation for part 866 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

■ 2. Add § 866.3958 to subpart D to read as follows:

§ 866.3958 Human immunodeficiency virus (HIV) viral load monitoring test.

(a) *Identification.* A human immunodeficiency virus (HIV) viral load monitoring test is an in vitro diagnostic prescription device for the quantitation of the amount of HIV RNA in human body fluids. The test is intended for use in the clinical management of individuals living with HIV and is for professional use only. The test results are intended to be interpreted in conjunction with other relevant clinical and laboratory findings. The test is not intended to be used as an aid in diagnosis or for screening donors of blood or blood products or human cells, tissues, or cellular and tissue-based products (HCT/Ps).

(b) *Classification.* Class II (special controls). The special controls for this device are:

(1) The labeling must include:

(i) An intended use that states that the device is not intended for use as an aid in diagnosis or for use in screening donors of blood or blood products, or HCT/Ps.

(ii) A detailed explanation of the principles of operation and procedures used for assay performance.

(iii) A detailed explanation of the interpretation of results and recommended actions to take based on current clinical guidelines.

(iv) Limitations, which must be updated to reflect current clinical practice and patient management. The limitations must include, but are not limited to, statements that indicate:

(A) The matrices and sample types with which the device has been cleared and that use of this test with specimen types other than those specifically cleared for this device may cause inaccurate test results.

(B) Mutations in highly conserved regions may affect binding of primers and/or probes resulting in the under-quantitation of virus or failure to detect the presence of virus.

(C) All test results should be interpreted in conjunction with the individual's clinical presentation, history, and other laboratory results.

(2) Device verification and validation must include:

(i) Detailed device description, including the device components, ancillary reagents required but not provided, and an explanation of the device methodology. Additional information appropriate to the technology must be included, such as detailed information on the design of primers and probes.

(ii) For devices with assay calibrators, the design and nature of all primary, secondary, and subsequent quantitation standards used for calibration as well as their traceability to a reference material. In addition, analytical testing must be performed following the release of a new lot of the standard material that was used for device clearance, or when there is a transition to a new calibration standard.

(iii) Detailed documentation of analytical performance studies conducted as appropriate to the technology, specimen types tested, and intended use of the device, including but not limited to, limit of blank, limit of detection, limit of quantitation, cutoff determination, precision, linearity, endogenous and exogenous interferences, cross-reactivity, carry-over, quality control, matrix equivalency, sample and reagent stability. Samples selected for use in analytical studies or used to prepare samples for use in analytical studies must be from subjects with clinically relevant genotypes circulating in the United States.

(iv) Multisite reproducibility study that includes the testing of three independent production lots.

(v) Analytical sensitivity of the device must demonstrate acceptable performance at current clinically relevant medical decision points. Samples tested to demonstrate analytical sensitivity must include appropriate numbers and types of samples, including real clinical samples near the lower limit of quantitation and any clinically relevant medical decision points. Analytical specificity of the device must demonstrate acceptable performance. Samples tested to demonstrate analytical specificity must include appropriate numbers and types of samples from patients with different underlying illnesses and infection and from patients with potential interfering substances.

(vi) Detailed documentation of performance from a multisite clinical study or a multisite analytical method comparison study.

(A) For devices evaluated in a multisite clinical study, the study must use specimens from individuals living with HIV being monitored for changes in viral load, and the test results must be compared to the clinical status of the patients.

(B) For tests evaluated in a multisite analytical method comparison study, the performance of the test must be compared to an FDA-cleared or approved comparator. The multisite method comparison study must include appropriate numbers and types of samples with analyte concentrations across the measuring range of the assay, representing clinically relevant genotypes. The multisite method comparison study design, including number of samples tested, must be sufficient to meet the following criteria:

(*1*) Agreement between the two tests across the measuring range of the assays must have an r2 of greater than or equal to 0.95.

(*2*) The bias between the test and comparator assay, as determined by difference plots, must be less than or equal to 0.5 log copies/mL.

(vii) If a multisite clinical study is performed under paragraph (b)(2)(vi) of this section, detailed documentation of a single-site analytical method comparison study between the device and an FDA-cleared or approved comparator. The analytical method comparison study must use appropriate numbers and types of samples with analyte concentrations across the measuring range of the assay, representing clinically relevant genotypes. The results must meet the criteria in paragraphs (b)(2)(vi)(B)(*1*) and (*2*) of this section.

(viii) Strategies for detection of new strains, types, subtypes, genotypes, and genetic mutations as they emerge.

(ix) Risk analysis and management strategies, such as Failure Modes Effects Analysis and/or Hazard Analysis and Critical Control Points summaries and their impact on test performance.

(x) Final release criteria to be used for manufactured device lots with an appropriate justification that lots released at the extremes of the specifications will meet the claimed analytical and clinical performance characteristics as well as the stability claims.

(xi) All stability protocols, including acceptance criteria.

(xii) Appropriate and acceptable procedure(s) for addressing complaints and other device information that determines when to submit a medical device report.

(xiii) Premarket notification submissions must include the information contained in paragraphs (b)(2)(i) through (xii) of this section.

Dated: November 16, 2021.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2021–25372 Filed 11–23–21; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HOMELAND SECURITY

Coast Guard

33 CFR Part 117

[Docket No. USCG–2021–0778]

RIN 1625–AA09

Drawbridge Operation Regulation; Willamette River, Portland, OR

AGENCY: Coast Guard, Department of Homeland Security (DHS).

ACTION: Notice of proposed rulemaking.

SUMMARY: The Coast Guard proposes to modify the operating schedule that governs the Morrison Bridge across the Willamette River, mile 12.8, at Portland, OR. Multnomah County, Oregon, the bridge owner, is requesting to change the current regulation to allow painting and preservation of the Morrison Bridge including the double bascule span. The modified rule would change from a full span opening to a single leaf, half opening, and operation. We invite your comments on this proposed rulemaking.

DATES: Comments and related material must reach the Coast Guard on or before December 27, 2021. The Coast Guard anticipates that this proposed rule will be effective from 7 p.m. on April 1, 2022, through 7 p.m. on May 31, 2023.

ADDRESSES: You may submit comments identified by docket number USCG–2021–0778 using Federal Decision Making Portal at *https://www.regulations.gov.* See the ''Public Participation and Request for Comments'' portion of the **SUPPLEMENTARY INFORMATION** section below for instructions on submitting comments.

FOR FURTHER INFORMATION CONTACT: If you have questions on this proposed rule, call or email Steven Fischer, Thirteenth District Bridge Administrator, U.S. Coast Guard; telephone 206–220–7282, email *d13-smb-d13-bridges@uscg.mil.*

SUPPLEMENTARY INFORMATION:

I. Table of Abbreviations

CFR Code of Federal Regulations
DHS Department of Homeland Security
FR Federal Register
OMB Office of Management and Budget
NPRM Notice of proposed rulemaking (Advance, Supplemental)
§ Section
U.S.C. United States Code
County Multnomah County

II. Background, Purpose and Legal Basis

Multnomah County, Oregon, owns and operates the Morrison Bridge across the Willamette River at mile 12.8. The County is requesting a temporary change to the existing operating regulation. The County is proposing to open the Morrison Bridge's span in single leaf mode, half of the double bascule span, to marine vessels with a minimum of two-hour notice, or four-hour notice if a tug assist is needed. The County needs to maintain half of the draw closed to allow for preservation and paint efforts. The proposed regulation change would allow the Morrison Bridge to alternate operation of the east or west leaf span from April 1, 2022, through May 31, 2023. The west span will be operational at the beginning of construction and the east span will be closed to navigation. The dates to switch operational spans will be determined later and published in the Local and Broadcast Notice to Mariners. This proposal also allows a containment system under the bridge that reduces the non-opening half of the bridge's vertical clearance by 5 feet from 69 feet center to 64 feet, and from 48 feet on the sides to 43 feet above the Columbia River Datum 0.0. Marine traffic on this section of the Willamette River consists of vessels ranging from small pleasure craft up to large commercial vessels and barges. The subject bridge currently operates in accordance with 33 CFR 117.897(c)(3)(iv).

III. Discussion of Proposed Rule

The Coast Guard proposes a temporary change to 33 CFR 117.897(c)(3)(iv) to be in effect from 7 p.m. on 1 April, 2022, through 7 p.m. on 31 May, 2023. This temporary rule will suspend the current regulatory cite regarding the Morrison Bridge, and add a temporary 33 CFR 117.897(c)(3)(vi) which will amend the operating schedule of the Morrison Bridge by requiring a two-hour notice, or four-hour notice with tug assist, for all draw openings, and alternate the operation of the double bascule spans to single span which will reduce the horizontal clearances of the bridge. The temporary rule is necessary to accommodate preservation and painting of the Morrison Bridge. This bridge provides a vertical clearance approximately 69 feet, at the center, above Columbia River Datum 0.0 when in the closed-to-navigation position. One half of the bascule bridge will have a containment system installed on the non-opening half of the span, which will reduce the vertical clearance by 5 feet to 64 feet center and 43 feet on the sides. A tug will be available for assists to mariners as needed when a request is given with a notice of four hours for an opening. The horizontal clearance with a full opening is 185 feet, therefore, in single leaf operations, a temporary rule change will reduced the horizontal clearance to approximately 90 feet. Vessels able to transit under the Morrison Bridge without an opening may do so at any time. Marine vessels are advised to be aware of fall hazards. This section of the Willamette River has no alternate routes. During the Portland Rose Festival, both leafs of the double bascule span will be fully operational. If any mariner submits a full opening request to the County prior to construction beginning, a full opening can be scheduled. All marine emergency vessels can navigate under the Morrison Bridge without an opening, and therefore do not need to contact the Hawthorne Bridge for an emergency opening.

This regulatory action determination is based on the ability of the Morrison Bridge to open on signal after the Hawthorne Bridge, at Willamette River mile 13.1, has received at least a two-hour notice, or four-hour notice for tug assist, by telephone at 503–988–3452 or VHF radio request. The Coast Guard has made this finding based on the fact that the proposed change allows any vessel needing a drawbridge opening to transit through the Morrison Bridge after providing adequate notice and being provided with tug assistance if required.