| AIRAC date | State | City | Airport | FDC No. | FDC date | Subject |
|---|---|---|---|---|---|---|
| 16–Jun–22 | OR | Redmond | Roberts Fld | 2/8524 | 4/25/22 | ILS OR LOC RWY 23, Amdt 5. |
| 16–Jun–22 | OR | Redmond | Roberts Fld | 2/8525 | 4/25/22 | RNAV (GPS) Z RWY 29, Amdt 1A. |
| 16–Jun–22 | TX | Austin | Austin Exec | 2/8614 | 4/15/22 | RNAV (GPS) RWY 13, Orig-A. |
| 16–Jun–22 | ID | Grangeville | Idaho County | 2/8625 | 4/25/22 | RNAV (GPS) RWY 26, Orig. |
| 16–Jun–22 | TX | Beaumont | Beaumont Muni | 2/8948 | 4/18/22 | RNAV (GPS) RWY 13, Amdt 1. |
| 16–Jun–22 | TX | Beaumont | Beaumont Muni | 2/8953 | 4/18/22 | RNAV (GPS) RWY 31, Amdt 1. |
| 16–Jun–22 | TX | Ennis | Ennis Muni | 2/9668 | 4/21/22 | VOR/DME–A, Amdt 1A. |
| 16–Jun–22 | PA | Butler | Pittsburgh/Butler Rgnl | 2/9976 | 3/29/22 | RNAV (GPS) RWY 26, Amdt 2. |

[FR Doc. 2022–10443 Filed 5–13–22; 8:45 am]

BILLING CODE 4910–13–P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

### 21 CFR Part 866

**[Docket No. FDA–2019–N–5192]**

## Microbiology Devices; Reclassification of Human Immunodeficiency Virus Serological Diagnostic and Supplemental Tests and Human Immunodeficiency Virus Nucleic Acid Diagnostic and Supplemental Tests

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final amendment; final order.

**SUMMARY:** The Food and Drug Administration (FDA, we, or the Agency) is issuing a final order to reclassify certain human immunodeficiency virus (HIV) serological diagnostic and supplemental tests and HIV nucleic acid (NAT) diagnostic and supplemental tests, postamendments class III devices with the product code MZF, into class II (special controls), subject to premarket notification. Through this final order, FDA is also adding two new device classification regulations and identifying special controls that the Agency believes are necessary to provide a reasonable assurance of safety and effectiveness for these device types. This final order will reduce the regulatory burdens associated with these device types, as manufacturers will no longer be required to submit a premarket approval application (PMA) but can instead submit a premarket notification (510(k)) and receive clearance before marketing their device.

**DATES:** This order is effective June 15, 2022.

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

**SUPPLEMENTARY INFORMATION:**

### I. Background—Regulatory Authorities

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended, 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).

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.

On February 21, 2020, FDA published in the **Federal Register** a proposed order (85 FR 10110) to reclassify certain HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests from class III to class II (special controls), subject to premarket notification. The comment period on the proposed order closed on April 21, 2020.

### II. Comments on the Proposed Order

In response to the February 21, 2020, proposed order, FDA received several comments from public health organizations, device manufacturers, and individuals by the close of the comment period, each containing one or more comments on one or more issues. We describe and respond to the comments in this section of the document. The order of response to the comments is purely for organizational purposes and does not signify the comment's value or importance nor the order in which the comments were received.

(Comment 1) Nearly all comments expressed general support for the proposed reclassification along with appropriate controls to assure safety and efficacy. The comments noted that reclassification could improve access to HIV testing, support earlier diagnosis and facilitate prevention of HIV, enhance laboratory efficiency and patient management, and strengthen public health surveillance.

(Response 1) We acknowledge and appreciate the supportive comments. We are reclassifying these devices and establishing the special controls published in the proposed order with some clarifications and modifications, as summarized in section III.

(Comment 2) Several comments recommended the reclassification of HIV viral load monitoring tests, which were not included within the scope of the proposed order. The comments expressed differing opinions regarding whether HIV viral load reclassification should be included in this final order. One comment also noted that, at the 119th meeting of the Blood Products Advisory Committee (BPAC) held on July 19, 2018 (the Panel), there was clear support from the committee for reclassification of HIV viral load monitoring tests.

(Response 2) We appreciate the comments and note that FDA published

a proposed order to reclassify HIV viral load monitoring tests from class III into class II on November 24, 2021 (86 FR 66982). HIV viral load monitoring tests have different intended uses than HIV serological and NAT diagnostic tests and raise different issues of safety and effectiveness. We do not think it is appropriate to reclassify HIV viral load monitoring tests in this final order without providing the public with the opportunity to comment on the basis of the proposed reclassification or on the special controls. Thus, we are proceeding with finalizing reclassification of HIV serological and NAT diagnostic and supplemental tests and are separately pursuing reclassification of HIV viral load tests.

(Comment 3) One comment recommended reclassification of home-use HIV diagnostic devices and stated that reclassification of such tests from class III to class II would encourage manufacturers to develop new tests for home use, which could help address current gaps and barriers to testing in certain populations. However, another comment did not support reclassification of HIV tests intended for home use.

(Response 3) FDA has approved only one home-use HIV diagnostic test to date, which is indicated as an in vitro diagnostic home-use test for detecting HIV (HIV–1 and HIV–2) in oral fluid. A positive result is preliminary and followup confirmatory testing is needed. As noted by one of the comments, home-use HIV diagnostic tests were not within the scope of the proposed order, and there are distinct performance considerations and risks associated with home-use HIV diagnostic tests. Thus, FDA does not intend to reclassify home-use HIV diagnostic tests at this time, and such devices are not included in the scope of this final order.

(Comment 4) Several comments, while generally expressing support for the proposed reclassification of HIV serological and NAT diagnostic and supplemental tests from class III to class II, expressed concerns regarding the proposed special controls on clinical sensitivity and specificity:

- *Performance of Currently Approved HIV Diagnostic Tests:* The comments stated that currently approved tests may not perform at the level specified in the special controls. One comment said that ''none of the currently approved assays perform at the level specified by the special controls.'' Another comment said that during the July 19, 2018, Panel meeting, it was noted that ''many of the currently approved assays don't actually perform at these levels.''
- *Performance Levels—Harmonization with Hepatitis C Virus (HCV) Tests:* Several comments expressed concerns about the proposed sensitivity and specificity levels for HIV tests being too stringent in general and not harmonized with those proposed for HCV tests. Others suggested that the proposed performance levels for sensitivity and specificity were inconsistent with the discussion at the July 19, 2018, Panel meeting. One of these comments recommended that the performance measure level of stringency should be a point estimate of 99 percent with a 95 percent lower bound of the 95 percent confidence interval and noted that the proposed special controls currently require a lower bound of the 95 percent confidence interval greater than or equal to 99 percent.
- *Characterization of Performance Measures—Harmonization with HCV Tests:* One comment indicated that, in order to harmonize HCV test requirements and HIV serologic and nucleic acid test requirements, the HIV test performance measures should be characterized as Positive Percent Agreement and Negative Percent Agreement with a predicate assay, rather than clinical sensitivity and specificity (*i.e.,* comparing the performance of antibody tests with other antibody tests, rather than with the presence or absence of disease).
- *Sample Size:* Two comments noted the investment needed to conduct clinical trials with sufficiently large sample size to demonstrate the required levels of sensitivity and specificity will serve as a disincentive for manufacturers to develop new assays or to adapt existing assays and will ultimately not meet the reclassification goal of improving access to quality HIV testing. The comments noted that sensitivity and specificity requirements, with related sample size needs, are one of the main driving forces of clinical trial cost.

(Response 4) We disagree with the comments regarding the performance of currently approved diagnostic tests, harmonization with HCV performance levels, and clinical trial sample size. FDA's experience with HIV diagnostic and supplemental tests demonstrates that the proposed criteria are consistent with the performance demonstrated by currently approved tests, which have a long history of safe and effective use. There may be, under some circumstances, differences observed in the performance of a test when used in a real-world setting and its performance in the more controlled environment of a clinical study. However, FDA believes that lowering the criteria for clinical study performance raises the risk that future devices will not provide the same level of safety and effectiveness as currently approved devices and, thus, will not provide a reasonable assurance of safety and effectiveness. The comments indicating that ''none of the currently approved assays perform at the level specified by the special controls'' and that ''many of the currently approved assays don't actually perform at these levels'' are inaccurate; all currently approved HIV diagnostic tests met or exceeded FDA's proposed criteria in the primary clinical studies submitted for approval.

FDA does not consider the sensitivity or specificity of tests meeting a 95 percent lower bound confidence interval of 95 percent to be equivalent to the sensitivity or specificity of tests meeting a lower bound of 99 percent. Tests that are unable to meet FDA's criteria in the special controls could potentially generate a much higher number of incorrect results than tests that meet FDA's proposed criteria. This risk is present with the lower bound of 95 percent even if the point estimate is constrained to 99 percent. Thus, introduction into the market of new HIV tests with decreased performance compared with currently available tests may result in a large increase in the number individuals who would receive incorrect results. Incorrect test results, both false positive and false negative results, endanger both individual and public health because people may undergo unneeded treatment or may be denied needed treatment and may inadvertently spread HIV.

Regarding aligning the proposed performance criteria with the performance criteria proposed as special controls for certain HCV antibody tests and nucleic acid-based HCV ribonucleic acid (RNA) tests, the performance necessary to provide a reasonable assurance of safety and effectiveness of an in vitro diagnostic device is based on, among other things, the specific analyte measured, the disease or condition for which the particular device is intended to be used in diagnosis, and the conditions of use. This means that the performance criteria identified in special controls may vary between devices that measure different analytes (*e.g.,* HIV and HCV) or with different conditions of use (*e.g.,* point of care (PoC) versus lab-based) because the risks associated with each device are different.

The performance criteria FDA proposed and finalized for HCV antibody tests and nucleic acid-based HCV RNA tests have been demonstrated to provide a reasonable assurance of

safety and effectiveness of these tests that aid in the diagnosis of HCV infection (see 85 FR 18483, April 2, 2020, and 86 FR 66173, November 22, 2021); likewise, the criteria FDA proposed for HIV diagnostic and supplemental tests have been demonstrated to provide a reasonable assurance of safety and effectiveness for these tests that aid in diagnosis of infection with HIV. Lowering performance criteria for HIV diagnostic and supplemental tests raises the risk that lower-performing tests, for which there is not a reasonable assurance of safety and effectiveness, will be on the market. Therefore, the performance criteria FDA is finalizing in this order do not mirror those FDA has finalized for HCV tests.

With respect to the concerns expressed about the number of samples that will be needed to conduct the clinical studies, we note that the final special controls do not specify a minimum number of samples that must be used. The number of samples needed in the study is dependent on the performance of the assay. Although reclassification of these devices to class II may not always result in smaller clinical studies than were conducted for HIV diagnostic and supplemental tests approved under PMAs, we believe that other effects of the reclassification of these devices into class II, such as typically shorter review timelines for 510(k) submissions, will decrease the burden associated with obtaining marketing authorization of these devices. For all the reasons mentioned above, FDA is retaining the proposed specificity and sensitivity performance criteria in this final order.

(Comment 5) Several comments addressed the special control to submit a complaint log to FDA. One comment requested clarification on which devices would be subject to the special control, the timeframe for submission of the complaint log, and how FDA will act on the information included in the complaint log. One comment indicated that this information will duplicate the information submitted under part 803 (21 CFR part 803), which requires the submission of malfunction reports. Another comment stated that the required submission of a complaint log to monitor decreases in test performance, manufacturing failures, or trends in false positive results is redundant and an unnecessary mitigation measure, and that current postmarket controls for complaint handling, trending, and safety reporting are sufficient to mitigate these risks and are subject to routine inspection. The comment further asserted that this special control would impose reporting requirements that are typically reserved for class III devices.

(Response 5) The submission of the complaint log to FDA is not intended to act as a replacement for a periodic report that is submitted for a PMA-approved device under 21 CFR 814.84 or to duplicate the information submitted to fulfill the requirements for medical device reports (MDRs) under part 803. Instead, we are requiring the submission of a log of the complaints a manufacturer receives about these devices that includes certain available information for each complaint. These complaints must already be reviewed and evaluated by manufacturers under 21 CFR 820.198. Therefore, we expect that submission of this log to FDA should not be burdensome to manufacturers. We have revised the special controls in this final order to clarify that the information about each complaint listed at §§ 866.3956(b)(1)(iii) and 866.3957(b)(1)(iii) (21 CFR 866.3956(b)(1)(iii) and 866.3957(b)(1)(iii)) must be included in the log to the extent it is available and that the types of complaints listed in the parenthetical are examples of the types of complaints manufacturers may receive about these devices.

Manufacturers may submit the information electronically through the FDA Electronic Submission Gateway or on paper or electronic media (*e.g.,* CD, DVD) to the Center for Biologics Evaluation and Research Document Control Center. The complaint log must be submitted only for a period of 5 years following device clearance. The requirement does not apply to devices previously approved by FDA following submission of a PMA application. However, if a manufacturer of a device previously approved under a PMA subsequently submits a traditional 510(k) for a change to that device, the requirement in the special controls would apply. The 5-year period does not restart because of minor changes to a device that do not necessitate the submission of a new 510(k). FDA intends to review the information submitted in the complaint logs in a timely way and engage with manufacturers as necessary.

The submission of the complaint log to FDA as required in the special control will alert FDA to potential problems with devices that may not meet the definition of MDR reportable events under part 803, but that can potentially affect the safety and effectiveness of these devices. Such problems may include an unusually high invalid rate or issues with users conducting the test. The submission of the complaint log will allow FDA to be alerted earlier to these concerns and to whether they have been adequately addressed, which we believe is important to providing reasonable assurance of safety and effectiveness for these devices. The Agency usually would not evaluate this kind of complaint information until an FDA inspection, which typically occurs less frequently than annually.

(Comment 6) Two comments indicated that the cost of conducting clinical trials to meet the performance requirements in the proposed special controls for HIV diagnostic and supplemental tests as compared to those proposed for HCV tests will be a disincentive for manufacturers to develop multiplex laboratory assays or dual point-of-care assays with both analytes. It was noted that, with the high burden of co-occurring HIV and HCV infection, the capability to fully and efficiently integrate diagnostic testing for HIV and HCV is essential.

(Response 6) FDA supports efforts to integrate diagnostic testing for HIV and HCV. However, as noted in Response 4 of this final order, the performance necessary to provide a reasonable assurance of safety and effectiveness of in vitro diagnostic devices is based on, among other things, the analyte, the disease or condition for which the particular device is intended to be used in diagnosis, and the conditions of use. Accordingly, the performance criteria necessary to provide a reasonable assurance of safety and effectiveness for an HIV diagnostic or supplemental test are reflected in this final order. Device manufacturers with questions on their plans for development of multiplex devices for HIV and HCV, including on the design of clinical studies, can request FDA feedback through the Q-Submission Program (Ref. 1).

(Comment 7) One comment noted that the proposed reclassification of HIV diagnostic and supplemental tests from class III to class II with special controls decreases some regulatory burden, including the reduced costs associated with a 510(k), compared to a PMA and supplements. However, the comment expressed concern that considerable burden remains associated with the cost of clinical trials to demonstrate the required performance criteria and to add a new specimen type, for example a dried blood spot, to a marketed device. The comment asserted that the clinical trial required to add a new specimen type under the proposed regulatory pathway would be equivalent to the current pathway and would be a disincentive to manufacturers to address changing needs in the field by

submitting changes to their original submission.

(Response 7) FDA concurs that reclassification of HIV diagnostic and supplemental tests from class III to class II with special controls will reduce regulatory burdens as manufacturers will no longer be required to submit a PMA but can instead submit a 510(k) and receive clearance before marketing their device. However, we decline to revise the special controls necessary to provide a reasonable assurance of safety and effectiveness of these devices for the reasons discussed in Response 4 above. FDA remains open to discussions with device manufacturers about clinical study designs.

(Comment 8) One comment objected to requiring prescriptions for HIV diagnostic testing, noting that the requirement would result in more HIV transmissions.

(Response 8) FDA believes that the reclassification of HIV diagnostic and supplemental tests to class II with special controls will provide a reasonable assurance of safety and effectiveness of these devices while expanding access to HIV testing and reducing the regulatory burden on manufacturers. Under this final order, the HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests subject to this reclassification are identified as prescription use only devices. There are different performance considerations and risks associated with non-prescription HIV diagnostic and supplemental tests. Although not subject to this final order, FDA has approved one home-use device for which a prescription is not required.

## III. Final Order

Based on the information discussed in the preamble to the proposed order (85 FR 10110), the comments received on the proposed order, the Panel discussions (Ref. 2), and FDA's experiences over the years with these device types, FDA concludes that special controls, in conjunction with general controls, will provide reasonable assurance of the safety and effectiveness of HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests. FDA is adopting its findings under section 513(f)(3) of the FD&C Act, as published in the preamble to the proposed order (85 FR 10110).

FDA is issuing this final order to reclassify certain HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests from class III into class II and to establish special controls that will be codified at §§ 866.3956 and 866.3957.[1] In this final order, the Agency has identified special controls under section 513(a)(1)(B) of the FD&C Act which, together with general controls, provide a reasonable assurance of the safety and effectiveness of HIV serological and NAT diagnostic and supplemental tests.

FDA is making a few clarifications and modifications to the special controls as published in the proposed order after considering public comments, as discussed above, and on its own initiative. These include: (1) Correcting a reference to ''prescription use only'' in § 866.3957(a) to read ''for professional use only'' and moving the placement of the text stating the tests are for professional use only within both §§ 866.3956(a) and 866.3957(a); (2) referring to ''blood products'' instead of ''plasma'' in § 866.3956(a) and (b)(1)(i)(A) and in § 866.3957(a) and (b)(1)(i)(A) for consistency with the labeling of more recently approved tests; (3) clarifying in §§ 866.3956(b)(1)(v)(A) and 866.3957(b)(1)(v)(A) that multisite clinical studies required for devices intended for PoC use must be conducted at appropriate PoC sites; (4) clarifying that the procedures for determining when to submit an MDR described in § 866.3956(b)(1)(ii)(K) and in § 866.3957(b)(1)(ii)(K) must be appropriate and acceptable so that they ensure appropriate adverse event reporting; (5) clarifying certain aspects of the special controls regarding submission of complaint log; (6) adding references to ''labeling'' in § 866.3956(b)(2), (b)(3), and (b)(5) and in § 866.3957(b)(2), (b)(3), and (b)(5) to make clearer that certain required statements must be included in the device labeling and making other minor wording changes to labeling statements required under §§ 866.3956(b)(2) and 866.3957(b)(2); (7) changing references to the PoC or supplemental ''claim'' to ''PoC use'' or ''supplemental use'' for consistency with terminology used elsewhere in the special controls; and (8) identifying more clearly that certain information must be included in 510(k) submissions for HIV diagnostic and supplemental 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 Act if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device. FDA has determined that premarket notification is necessary to provide a reasonable assurance of the safety and effectiveness of HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests. Therefore, these device types are not exempt from premarket notification requirements. Persons who intend to market theses device types must submit and obtain clearance of a premarket notification and demonstrate compliance with the special controls in this final order, prior to marketing the device.

The devices that are the subject of this reclassification are assigned the generic names ''human immunodeficiency virus (HIV) serological diagnostic and supplemental tests'' and ''human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and supplemental tests.'' HIV serological diagnostic and supplemental tests are identified as prescription devices for the qualitative detection of HIV antigen(s) and/or detection of antibodies against HIV in human body fluids or tissues. HIV NAT diagnostic and supplemental tests are identified as prescription devices for the qualitative detection of HIV nucleic acid in human body fluids or tissues. HIV serological diagnostic and supplemental tests and the NAT diagnostic and supplemental tests are intended for use as an aid in the diagnosis of infection with HIV, and their results are intended to be interpreted in conjunction with other relevant clinical and laboratory findings. These tests are for professional use only and are not intended to be used for monitoring patient status or for screening donors of blood or blood products, or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

Under this final order, the HIV serological diagnostic and supplemental tests and HIV NAT diagnostic and supplemental tests are identified as prescription use only devices. Prescription in vitro diagnostic devices are exempt from the requirement for adequate directions for use under section 502(f)(1) of the FD&C Act (21 U.S.C. 352(f)(1)) and 21 CFR 801.5, as long as all the conditions of 21 CFR 801.109 are met. A premarket notification submission for these devices will be required in the circumstances described in 21 CFR 807.81.

[1] FDA notes that the ''ACTION'' caption for this final order is styled as ''Final amendment; final order,'' rather than ''Final order.'' Beginning in December 2019, this editorial change was made to indicate that the document ''amends'' the Code of Federal Regulations. This 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.

## IV. 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. In accordance with section 513(f)(3) of the FD&C Act, we are codifying in this final order the classification of HIV serological diagnostic and supplemental tests in the new § 866.3956, under which these devices are reclassified from class III to class II. In addition, we are codifying the classification of HIV NAT diagnostic and supplemental tests in the new § 866.3957, under which these devices are reclassified from class III to class II.

## V. 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.

## VI. Paperwork Reduction Act of 1995

This final order contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The information collection provisions in §§ 866.3956(b)(1)(iii) and 866.3957(b)(1)(iii) have been approved under OMB control number 0910–0437. This approval expires on March 31, 2025. An Agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

This final order also 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 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.

## VII. References

The following references are on display in 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. FDA, ''Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program,'' available at *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program.*
2. Transcript of the July 19, 2018, Meeting of the Blood Products Advisory Committee (BPAC), available at: *https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/BloodProductsAdvisoryCommittee/ucm597841.htm.*

## List of Subjects in 21 CFR Part 866

Biologics, Laboratories, Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 866 is 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 § 866.3956 to subpart D to read as follows:

### § 866.3956 Human immunodeficiency virus (HIV) serological diagnostic and/or supplemental test.

(a) *Identification.* Human immunodeficiency virus (HIV) serological diagnostic and supplemental tests are prescription devices for the qualitative detection of HIV antigen(s) and/or detection of antibodies against HIV in human body fluids or tissues. The tests are intended for use as an aid in the diagnosis of infection with HIV and are for professional use only. The test results are intended to be interpreted in conjunction with other relevant clinical and laboratory findings. These tests are not intended to be used for monitoring patient status, or for screening donors of blood or blood products, or human cells, tissues, and cellular and tissue-based products (HCT/Ps).

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

(1) For all HIV serological diagnostic and supplemental tests

(i) The labeling must include:

(A) An intended use that states that the device is not intended for use for screening donors of blood or blood products or HCT/Ps.

(B) A detailed explanation of the principles of operation and procedures used for performing the assay.

(C) A detailed explanation of the interpretation of results and recommended actions to take based on results.

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

*(1)* The matrices with which the device has been cleared, and that use of this test kit with specimen types other than those specifically cleared for this device may result in inaccurate test results.

*(2)* The test is not intended to be used to monitor individuals who are undergoing treatment for HIV infection.

*(3)* A specimen with a reactive result should be investigated further following current guidelines.

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

*(5)* A test result that is nonreactive does not exclude the possibility of exposure to or infection with HIV. Nonreactive results in this assay may be due to analyte levels that are below the limit of detection of this assay.

(ii) Device verification and validation must include:

(A) Detailed device description, including the device components, ancillary reagents required but not provided, and an explanation of the methodology. Additional information appropriate to the technology must be included, such as the amino acid sequence of antigen(s) and design of capture antibodies.

(B) For devices with assay calibrators, the design 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.

(C) 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, cutoff determination, precision, endogenous and exogenous interferences, cross reactivity, carryover, quality control, matrix equivalency, and 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 circulating genotypes in the United States.

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

(E) Analytical sensitivity of the test must be the same as or better than that of other cleared or approved tests. Samples tested must include appropriate numbers and types of samples, including real clinical samples near the lower limit of detection. Analytical specificity of the test must be the same as or better than that of other cleared or approved tests. Samples must include appropriate numbers and types of samples from patients with different underlying illnesses or infections and from patients with potential endogenous interfering substances.

(F) Detailed documentation of performance from a multisite clinical study. Performance must be analyzed relative to an FDA-cleared or approved comparator. This study must be conducted using patient samples, with an appropriate number of HIV positive and HIV negative samples in applicable risk categories. Additional subgroups or types must be validated using appropriate numbers and types of samples. The samples may be a combination of fresh and repository samples, sourced from within and outside the United States, as appropriate. The study designs, including number of samples tested, must be sufficient to meet the following criteria:

*(1)* Clinical sensitivity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 99 percent.

*(2)* Clinical specificity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 99 percent.

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

(H) 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.

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

(J) All stability protocols, including acceptance criteria.

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

(L) Premarket notification submissions must include the information contained in paragraph (b)(1)(ii)(A) through (K) of this section.

(iii) Manufacturers must submit a log of all complaints. The log must include the following information regarding each complaint if available: The type of event (*e.g.,* false negative/false nonreactive or false positive/false reactive), lot, date, population, and whether or not the complaint was reported under part 803 of this chapter (Medical Device Reporting). The log must be submitted annually on the anniversary of clearance for 5 years following clearance of a traditional premarket notification.

(2) If the test is intended for Point of Care (PoC) use, the following special controls, in addition to those listed in paragraph (b)(1) of this section apply:

(i) The PoC labeling must include a statement that the test is intended for PoC use.

(ii) The PoC labeling must include the following information near the statement of the intended use:

(A) That the test is for distribution to clinical laboratories that have an adequate quality assurance program, including planned systematic activities that provide adequate confidence that requirements for quality will be met and where there is assurance that operators will receive and use the instructional materials.

(B) That the test is for use only by an agent of a clinical laboratory.

(C) Instructions for individuals to receive the ''Subject Information Notice'' prior to specimen collection and appropriate information when test results are provided.

(iii) PoC labeling must include instructions to follow current guidelines for informing the individual of the test result and its interpretation.

(iv) The instructions in the labeling must state that reactive results are considered preliminary and should be confirmed following current guidelines.

(v) Device verification and validation for PoC use must include:

(A) Detailed documentation of performance from a multisite clinical study conducted at appropriate PoC sites. Performance must be analyzed relative to an FDA cleared or approved comparator. This study must be conducted using patient samples, with appropriate numbers of HIV positive and HIV negative samples in applicable risk categories. Additional subgroup or type claims must be validated using appropriate numbers and types of samples. The samples may be a combination of fresh and repository samples, sourced from within and outside the United States, as appropriate. If the test is intended solely for PoC use, the test must meet only the performance criteria in paragraphs (b)(2)(v)(A)(*1*) and (*2*) of this section and not the criteria in paragraph (b)(1)(ii)(F) of this section:

*(1)* Clinical sensitivity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 98 percent.

*(2)* Clinical specificity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 98 percent.

(B) Premarket notification submissions must include the information contained in paragraph (b)(2)(v)(A) of this section.

(3) If the test is intended for supplemental use in addition to use as an aid in initial diagnosis, the following special controls, in addition to those listed in paragraphs (b)(1) and (2) of this section, as appropriate, apply:

(i) The labeling must include a statement that the test is intended for use as an additional test to confirm the presence of HIV antibodies or antigens in specimens found to be repeatedly reactive by a diagnostic screening test.

(ii) Device validation and verification for supplemental use must include a clinical study, including samples that were initially reactive and repeatedly reactive on a diagnostic test but were negative or indeterminate on a different confirmatory test. Premarket notification submissions must include this information.

(4) If the test is intended solely as a supplemental test, the following special controls, in addition to those listed in paragraphs (b)(1) and (2) of this section, except those in paragraphs (b)(1)(ii)(F) and (b)(2)(v)(A) of this section, as appropriate, apply:

(i) The labeling must include a statement that the test is intended for use as an additional test to confirm the presence of HIV antibodies or antigens in specimens found to be repeatedly reactive by a diagnostic screening test.

(ii) The labeling must clearly state that the test is not for use for initial diagnosis or is not intended as a first-line test.

(iii) Device validation and verification must include a clinical study including samples that were initially reactive and repeatedly reactive on a diagnostic test but were negative or indeterminate on a confirmatory test. Premarket notification submissions must include this information.

(5) If the test is intended to differentiate different HIV types, the following special controls, in addition to those listed in paragraphs (b)(1) through (4) of this section, as appropriate, apply:

(i) The labeling must include the statement that the test is intended for the confirmation of initial results from a diagnostic test and differentiation of different HIV types.

(ii) The results interpretation in the labeling must include instructions for the user on how to interpret the results, including un-typeable and co-infection results.

(iii) Device validation and verification must include evaluation of analytical and clinical sensitivity and specificity for each of the HIV types, strains, and subtypes of HIV intended to be differentiated. Premarket notification submissions must include this information.

■ 3. Add § 866.3957 to subpart D to read as follows:

**§ 866.3957 Human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and/or supplemental test.**

(a) *Identification.* Human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and supplemental tests are prescription devices for the qualitative detection of HIV nucleic acid in human body fluids or tissues. The tests are intended for use as an aid in the diagnosis of infection with HIV and are for professional use only. The test results are intended to be interpreted in conjunction with other relevant clinical and laboratory findings. These tests are not intended to be used for monitoring patient status, or for screening donors of blood or blood products, or human cells, tissues, or cellular or tissue-based products (HCT/Ps).

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

(1) For all HIV NAT diagnostic and/or supplemental tests

(i) The labeling must include:

(A) An intended use that states that the device is not intended for use for screening donors of blood or blood products, or HCT/Ps.

(B) A detailed explanation of the principles of operation and procedures used for performing the assay.

(C) A detailed explanation of the interpretation of results and recommended actions to take based on results.

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

*(1)* The matrices with which the device has been cleared, and that use of this test kit with specimen types other than those specifically cleared for this device may result in inaccurate test results.

*(2)* The test is not intended to be used to monitor individuals who are undergoing treatment for HIV infection.

*(3)* A specimen with a reactive result should be investigated further following current guidelines.

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

*(5)* A test result that is nonreactive does not exclude the possibility of exposure to or infection with HIV. Nonreactive results in this assay may be due to analyte levels that are below the limit of detection of this assay.

(ii) Device verification and validation must include:

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

(B) 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.

(C) 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, cutoff determination, precision, endogenous and exogenous interferences, cross reactivity, carryover, quality control, matrix equivalency, and 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 circulating genotypes in the United States. The effect of each claimed nucleic-acid isolation and purification procedure on detection must be evaluated.

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

(E) Analytical sensitivity of the test must be the same as or better than that of other cleared or approved tests. Samples tested must include appropriate numbers and types of samples, including real clinical samples near the lower limit of detection. Analytical specificity of the test must be as the same as or better than that of other cleared or approved tests. Samples must include appropriate numbers and types of samples from patients with different underlying illnesses or infections and from patients with potential endogenous interfering substances.

(F) Detailed documentation of performance from a multisite clinical study. Performance must be analyzed relative to an FDA cleared or approved comparator. This study must be conducted using appropriate patient samples, with appropriate numbers of HIV positive and negative samples in applicable risk categories. Additional subtype, strain, or types must be validated using appropriate numbers and types of samples. The samples may be a combination of fresh and repository samples, sourced from within and outside the United States, as appropriate. The study designs, including number of samples tested, must be sufficient to meet the following criteria:

*(1)* Clinical sensitivity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 99 percent.

*(2)* Clinical specificity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 99 percent.

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

(H) 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.

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

(J) All stability protocols, including acceptance criteria.

(K) Appropriate and acceptable procedure(s) for evaluating customer complaints and other device

information that determine when to submit a medical device report.

(L) Premarket notification submissions must include the information contained in paragraph (b)(1)(ii)(A) through (K) of this section.

(iii) Manufacturers must submit a log of all complaints. The log must include the following information regarding each complaint, if available: The type of event (*e.g.,* false negative/false nonreactive or false positive/false reactive), lot, date, population, and whether or not the complaint was reported under part 803 of this chapter (Medical Device Reporting). The log must be submitted annually on the anniversary of clearance for 5 years following clearance of a traditional premarket notification.

(2) If the test is intended for Point of Care (PoC) use, the following special controls, in addition to those listed in paragraph (b)(1) of this section, apply:

(i) The PoC labeling must include a statement that the test is intended for PoC use.

(ii) The PoC labeling must include the following information near the statement of the intended use:

(A) That the test is for distribution to clinical laboratories that have an adequate quality assurance program, including planned systematic activities that provide adequate confidence that requirements for quality will be met and where there is assurance that operators will receive and use the instructional materials.

(B) That the test is for use only by an agent of a clinical laboratory.

(C) Instructions for individuals to receive the ''Subject Information Notice'' prior to specimen collection and appropriate information when test results are provided.

(iii) PoC labeling must include instructions to follow current guidelines for informing the individual of the test result and its interpretation.

(iv) The instructions in the labeling must state that reactive results are considered preliminary and should be confirmed following current guidelines.

(v) Device verification and validation for PoC use must include:

(A) Detailed documentation from a well-conducted multisite clinical study conducted at appropriate PoC sites. Performance must be analyzed relative to an FDA cleared or approved comparator. This study must be conducted using patient samples, with appropriate numbers of HIV positive and HIV negative samples in applicable risk categories. Additional subgroup or type claims must be validated using appropriate numbers and types of samples. The samples may be a combination of fresh and repository samples, sourced from within and outside the United States, as appropriate. If the test is intended solely for PoC use, the test must meet only the performance criteria in paragraphs (b)(2)(v)(A)(*1*) and (*2*) of this section and not the criteria in paragraph (b)(1)(ii)(F) of this section:

*(1)* Clinical sensitivity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 98 percent.

*(2)* Clinical specificity of the test must have a lower bound of the 95 percent confidence interval of greater than or equal to 98 percent.

(B) Premarket notification submissions must include the information contained in paragraph (b)(2)(v)(A) of this section.

(3) If the test is intended for supplemental use in addition to use as an aid in initial diagnosis, the following special controls, in addition to those listed in paragraphs (b)(1) and (2) of this section, as appropriate, apply:

(i) The labeling must include a statement that the test is intended for use as an additional test to confirm the presence of HIV viral nucleic acid in specimens found to be repeatedly reactive by a diagnostic screening test.

(ii) Device validation and verification for supplemental use must include a clinical study, including samples that were initially reactive and repeatedly reactive on a diagnostic test but were negative or indeterminate on a confirmatory test. Premarket notification submissions must include this information.

(4) If the test is intended solely as a supplemental test, the following special controls, in addition to those listed in paragraphs (b)(1) and (2) of this section, except those in paragraphs (b)(1)(ii)(F) and (b)(2)(v)(A) of this section, as appropriate, apply:

(i) The labeling must include a statement that the test is intended for use as an additional test to confirm the presence of HIV viral nucleic acid in specimens found to be repeatedly reactive by a diagnostic screening test.

(ii) The labeling must clearly state that the test is not for use for initial diagnosis or is not intended as a first-line test.

(iii) Device validation and verification must include a clinical study including samples that were initially reactive and repeatedly reactive on a diagnostic test but were negative or indeterminate on a confirmatory test. Premarket notification submissions must include this information.

(5) If the test is intended to differentiate different HIV types, the following special controls, in addition to those listed in paragraphs (b)(1) through (4) of this section, as appropriate, apply:

(i) The labeling must include the statement that the test is intended for the confirmation of initial results and differentiation of different HIV types.

(ii) The results interpretation in the labeling must include instructions for the user on how to interpret the results, including un-typeable and co-infection results.

(iii) Device validation and verification must include evaluation of analytical and clinical sensitivity and specificity for each of the types, strains, and subtypes of HIV intended to be differentiated. Premarket notification submissions must include this information.

Dated: May 11, 2022.

**Lauren K. Roth,**

*Associate Commissioner for Policy.*

[FR Doc. 2022–10461 Filed 5–13–22; 8:45 am]

**BILLING CODE 4164–01–P**

## DEPARTMENT OF HOMELAND SECURITY

### Coast Guard

### 33 CFR Part 110

**[Docket Number USCG–2020–0154]**

**RIN 1625–AA01**

## Anchorage Regulations; Ten Anchorages on the Mississippi River Mile Markers 12–85 AHP

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

**ACTION:** Final rule.

**SUMMARY:** The Coast Guard is amending anchorage regulations for the Lower Mississippi River (LMR) between mile marker (MM) 12 above head of passes (AHP), to MM 85 AHP. This amendment modifies nine anchorage grounds and establishes one new anchorage ground. This regulation increases the available anchorage areas necessary to accommodate vessel traffic, promote navigational safety, provide for the overall safe and efficient flow of vessel traffic and commerce, and bolster the economy through increased anchorage capacity.

**DATES:** This rule is effective June 15, 2022.

**ADDRESSES:** To view documents mentioned in this preamble as being available in the docket, go to *https://www.regulations.gov,* type USCG–2020–0154 in the search box and click