August 16, 2024

NOWDiagnostics
% David Kern
Consultant
K2 Regulatory Consulting, LLC
479 Cumberland Drive
Burlingame, California 94010

Re: DEN230090
Trade/Device Name: First To Know Syphilis Test
Regulation Number: 21 CFR 866.3986
Regulation Name: Test for detection of antibodies associated with syphilis performed by lay users.
Regulatory Class: Class II
Product Code: SBZ
Dated: December 27, 2023
Received: December 27, 2023

Dear David Kern:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the First To Know Syphilis Test, an over-the-counter device with the following indications for use:

> The First To Know Syphilis Test is a qualitative rapid membrane immunochromatographic assay for the detection of *Treponema pallidum* (syphilis) antibodies in human whole blood (capillary). This test is intended for over the counter (OTC) consumer use in individuals suspected of syphilis. Positive test results with the First To Know Syphilis Test alone are not sufficient to diagnose syphilis infection and must be followed by additional laboratory testing through a health care provider to confirm a diagnosis of syphilis.
>
> This test is not a substitute for visits to a healthcare provider. The information provided by this product should not be used to start, stop or change any treatments without a healthcare provider.
>
> Results of testing with the First To Know Syphilis Test will likely be positive for individuals previously diagnosed with syphilis, even if they were successfully treated. The First To Know Syphilis Test cannot determine whether there has been re-infection with syphilis.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the First To Know Syphilis Test, and substantially equivalent devices of this generic type, into Class II under the generic name test for detection of antibodies associated with syphilis performed by lay users.

FDA identifies this generic type of device as:

> **Test for detection of antibodies associated with syphilis performed by lay users.** A test for detection of antibodies associated with syphilis performed by lay users is an in vitro diagnostic device used for detection of antibodies in clinical specimens for use in home settings, or similar environments. The device is intended to aid in diagnosis of syphilis and is intended for prescription or over-the-counter use.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. On December 13, 2016, the 21st Century Cures Act removed a requirement that a De Novo request be submitted within 30 days of receiving an NSE determination. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register announcing the classification.

On December 27, 2023, FDA received your De Novo requesting classification of the First To Know Syphilis Test. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the First To Know Syphilis Test into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the First To Know Syphilis Test can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Risks to Health	Mitigation Measures
Risk of false results	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures. Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.
Failure to correctly interpret test results	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures. Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.

Risks to Health	Mitigation Measures
Failure to correctly operate the device	Certain labeling information including limitations, device descriptions, performance information, and explanations of procedures. Certain design verification and validation including certain analytical and clinical studies, and risk analysis strategies.

In combination with the general controls of the FD&C Act, the test for detection of antibodies associated with syphilis performed by lay users is subject to the following special controls:

(1) The intended use in the labeling must include the following:
   (i) A description of the analytes the device detects, the specimen types tested, the results provided to the user, the clinical indications for which the test is to be used, the specific intended population(s), and other conditions of use, as appropriate;
   (ii) A statement that a positive result with this test alone is not sufficient to diagnose infection;
   (iii) A statement that results will likely be positive for individuals previously diagnosed with syphilis, even if they were successfully treated, as appropriate.

(2) Design verification and validation must include:
   (i) Detailed documentation from a prospective clinical study with a design and performance that is appropriate for the intended use of the device, including performance estimates derived from a sufficient number of samples from the intended use population. Results must be obtained from geographically diverse locations, include a spectrum of users with respect to age, education, and ethnicity and include population(s) with risk factors, including pregnant women and individuals with HIV, as appropriate. The clinical study must be performed in the intended use setting (i.e., at home or a home-like environment). The results obtained with the candidate device must be compared to results obtained using a comparator that FDA has determined to be appropriate. Detailed documentation must include the clinical study protocol (including a predefined statistical analysis plan), study report, testing results, and results of all statistical analyses;
   (ii) Detailed documentation of analytical studies, including determination of the assay cutoff, inclusivity, cross-reactivity with other antibodies, interfering substances, within-lab precision, hook effect, carryover/cross contamination, as applicable;
   (iii) Detailed documentation and characterization (e.g., determination of the identity, supplier, purity, and stability) of all critical reagents and protocols for maintaining product integrity throughout its labeled shelf-life, i.e., reagent stability studies. Data and protocols, including acceptance criteria, from a multi-lot reagent stability study must include testing of samples with challenging analyte concentration, and must include in-use/open-kit stability, as well as shipping stability under extreme environmental conditions (as applicable);
   (iv) Risk analysis and documentation demonstrating how risk control measures are implemented to address device system hazards, such as Failure Modes Effects Analysis and/or Hazard Analysis. This must include detailed documentation that demonstrates the effectiveness of risk control measures and device robustness, including the entire testing procedure from sampling to result interpretation, based on results from the following studies, as applicable per the intended use of the test device: usability studies, user label comprehension, and flex studies.

(3) Labeling must include the following:
   (i) Easy to follow step-by-step instructions written in appropriate language for the intended user, explanation of test results and results interpretation, including instructions on what actions to take based on the test results, and a Frequently Asked Questions (FAQs) section that provides technical and educational information, and information for technical assistance with the test;
   (ii) Limiting statements including the following, as applicable:
      (A) Statements that a negative test result does not preclude the possibility of infection with other pathogens, and that a positive test result does not preclude the possibility of co-infection with additional pathogens;
      (B) A statement that the test is not a substitute for visits to a healthcare provider. The result obtained with this test should not be used to start, stop, or change any course of treatment unless advised by their healthcare provider;
      (C) A statement that accurate results are dependent on adequate product storage, and adherence to the specimen collection and testing procedures, and failure to follow test procedures can lead to incorrect results;
      (D) A statement that anyone with recent sexual contact with a person known to have a sexually transmitted infection should visit a healthcare provider for treatment and evaluation as soon as possible;
      (E) A statement that this test is not intended to replace routine healthcare during pregnancy regardless of test results.

   (iii) The outer box label must include the following:
      (A) A list of the components required to run the test, but not provided;
      (B) A statement that anyone with recent sexual contact with a person known to have a sexually transmitted infection should visit a healthcare provider for evaluation and treatment as soon as possible;
      (C) A statement that results will likely be positive for individuals previously diagnosed with syphilis, even if they were successfully treated, as applicable.

Although this letter refers to your product as a device, please be aware that some granted products may instead be combination products. If you have questions on whether your product is a combination product, contact CDRHProductJurisdiction@fda.hhs.gov.

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 type. FDA has determined premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the test for detection of antibodies associated with syphilis performed by lay users they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD&C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD&C Act; 21 CFR 1000-1050).

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Mark Soboleski at 301-796-3298.

Sincerely,

Uwe Scherf -S

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