November 5, 2019

Vela Diagnostics USA Inc.
Attention: Mr. Donald Henton
353 C US Route 46 West, Suite 250
Fairfield, NJ 07004

Re:	BR190330
Trade Name:	*Sentosa*® SQ HIV Genotyping Assay
Regulation Number:	21 CFR 866.3955
Regulation Name:	Human immunodeficiency virus (HIV) drug resistance genotype assay using next generation sequencing (NGS) technology
Regulatory Class:	Class II
Product Code:	QIC
Dated:	October 29, 2019
Received:	October 29, 2019

Dear Mr. Henton:

The Center for Biologics Evaluation and Research (CBER) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the *Sentosa*® SQ HIV Genotyping Assay, a prescription device under 21 CFR Part 801.109 with the following indications for use:

> The *Sentosa*® SQ HIV-1 Genotyping Assay is a next generation sequencing (NGS)-based in vitro diagnostic (IVD) test intended for use in detecting HIV-1 genomic mutations (in the protease, reverse transcriptase and integrase regions of the pol gene) as an aid in monitoring and treating HIV-1 infection. This test is used in adjunct to the therapeutic management of patients diagnosed with HIV-1 Group M infection with viral loads of at least 1,000 RNA copies per mL in EDTA plasma specimens.
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> The *Sentosa*® SQ HIV-1 Genotyping Assay is used in conjunction with the *Sentosa*® SX Virus Total Nucleic Acid Plus (4x24) and *Sentosa*® SX IA Template Prep kits on the *Sentosa*® SX101 instrument, and *Sentosa*® SQ Sequencing instrument and *Sentosa*® SQ 318 Chip kit.
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> Results should be used in conjunction with other available laboratory and clinical information and are not intended for use as an aid in the diagnosis of infection with HIV or to confirm the presence of HIV infection, or for screening donors of blood, plasma or human cells, tissues and cellular and tissue-based products (HCT/Ps).

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. FDA concludes that this device should be classified into Class II. This order, therefore, classifies the *Sentosa*® SQ HIV Genotyping Assay, and substantially equivalent devices of this generic type, into Class II under the generic name Human immunodeficiency virus (HIV) drug resistance genotype assay using next generation sequencing (NGS) technology.

FDA identifies this generic type of device as:

> The human immunodeficiency virus (HIV) drug resistance genotyping assay using next generation sequencing (NGS) technology is a prescription in vitro diagnostic device intended for use in detecting HIV genomic mutations that confer resistance to specific anti-retroviral drugs. The device is intended to be used as an aid in monitoring and treating HIV infection.

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 March 19, 2019, FDA received your De Novo requesting classification of the *Sentosa*® SQ HIV Genotyping Assay. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the *Sentosa*® SQ HIV Genotyping Assay 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 *Sentosa*® SQ HIV Genotyping Assay 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:

Identified Risks	Mitigation Measures
Inaccurate detection of resistance mutation(s)	Device description information, including performance characteristics, and performance studies in labeling. Device description validation procedures and performance studies meeting acceptance criteria. Device limitations in labeling for genetic mutation detection.
Incorrect interpretation of test results	Device description information, performance characteristics, and performance studies in labeling.

In combination with the general controls of the FD&C Act, the Human immunodeficiency virus (HIV) drug resistance genotype assay using next generation sequencing (NGS) technology. This device is subject to the following special controls:

1. The intended use of the device must:

    a. Specify the analyte (RNA or DNA), the genes in which mutations are detected, the clinical indications appropriate for test use, the sample type, and the specific population(s) for which the device in intended.

    b. State that the device in not intended for use as an aid in the diagnosis of infection with HIV or to confirm the presence of HIV infection, or for screening donors of blood, plasma or human cells, tissues and cellular and tissue-based products (HCT/Ps).

2. The labeling must include:

    a. A detailed device description, including but not limited to, all procedures from collection of the patient sample to reporting the final result, all device components, the control elements incorporated into the test procedure, instrument requirements, and reagents required for use but not provided as part of the device.

    b. Performance characteristics from analytical studies and all intended specimen types.

    c. A list of specific mutations detected.

    d. The name and version of the standardized database used for sequence comparison and results derivation.

e. A detailed explanation of the interpretation of test results, including acceptance criteria for evaluating the validity of a test run.

f. A limitation statement that the device is intended to be used in conjunction with clinical history and other laboratory findings. Results of this test are intended to be interpreted by a physician or equivalent.

g. A limitation statement that lack of detection of drug resistance mutations does not preclude the possibility of genetic mutation.

h. A limitation statement indicating the relevant genetic mutations that are included in the standardized database of HIV genomic sequences used for comparison and results derivation but that are not detected by the test.

i. A limitation statement that detection of a genomic drug resistance mutation may not correlate with phenotypic gene expression.

j. A limitation statement that the test does not detect all genetic mutations associated with antiviral drugs.

k. A limitation statement listing the HIV types for which the test is not intended, if any.

3. Device verification and validation must include:

a. Design of primer sequences and rationale for sequence selection.

b. Computational path from collection of raw data to reported result.

c. Detailed documentation of analytical studies including, but not limited to, characterization of the cut-off, analytical sensitivity, inclusivity, reproducibility, interference, cross reactivity, instrument and method carryover/cross contamination, sample stability and handling for all genomic mutations claimed in the intended use.

d. Precision studies that include all genomic mutations claimed in the intended use.

e. Detailed documentation of a multisite clinical study evaluating the sensitivity and specificity of the device. Clinical study subjects must represent the intended use population and device results for all targets claimed in the intended use must be compared to Sanger sequencing or other methods found acceptable by FDA. Drug resistance-associated mutations at or above the 20 percent frequency level must detect the mutations in greater than 90 percent of at least 10 replicates, for each of drug class evaluated.

f. Documentation that variant calling is performed at a level of coverage that supports positive detection of all genomic mutations claimed in the intended use.

g. Detailed documentation of limit of detection studies (LoD) in which device performance is evaluated by testing a minimum of 100 HIV-positive clinical samples including samples with analyte concentrations near the clinical decision points and near the LoD.

    i. The LoD for the device must be determined using a minimum of 10 HIV-1 group M genotypes if applicable. A detection rate at 1x LoD greater than or equal to 95 percent must be demonstrated for mutations with a frequency greater than 20 percent.

    ii. The LoD of genetic mutations at frequency levels less than 20 percent must be established.

h. A predefined HIV genotyping bioinformatics analysis pipeline (BAP). The BAP must adequately describe the bioinformatic analysis of the sequencing data, including but not limited to read alignment, variant calling, assembly, genotyping, quality control and final result reporting.

i. A clear description of the selection and use of the standardized database that is used for sequence comparison and results derivation.

4. Premarket notification submissions must include the information in 3.a – i.

In addition, this is a prescription device and must comply with 21 CFR 801.109.

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 Human immunodeficiency virus (HIV) drug resistance genotype assay using next generation sequencing (NGS) technology 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); 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 questions concerning this letter, please contact the Regulatory Project Manager, Dr. Vasantha Kumar, at (240) 402-8413 or Vasantha.Kumar@fda.hhs.gov.

Sincerely,

Hira L. Nakhasi, PhD
Director
Division of Emerging and
Transfusion Transmitted Diseases
Office of Blood Research and Review
Center for Biologics Evaluation and Research

Enclosure: Indication For use