February 3, 2023

Estela Raychaudhuri
President
307 Westlake Ave N, Suite 300
Seattle, Washington 98109

Re: DEN220044
Trade/Device Name: Active Anthrax Detect Plus Rapid Test
Regulation Number: 21 CFR 866.3046
Regulation Name: Simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* species (spp.) in human clinical samples
Regulatory Class: Class II
Product Code: QUU
Dated: July 6, 2022
Received: July 8, 2022

Dear Estela Raychaudhuri:

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 Active Anthrax Detect Plus Rapid Test, a prescription device with the following indications for use:

> The Active Anthrax Detect Plus Rapid Test point-of-care diagnostic test for pulmonary anthrax is an *in vitro* immunochromatographic device for use as an aid in the diagnosis of inhalation anthrax. It provides visual and rapid qualitative detection of lethal factor of *Bacillus anthracis* (*B. anthracis*). The test can be used to test serum and venous whole blood (dipotassium EDTA, sodium citrate, and sodium heparin). The assay is indicated for testing samples from individuals who have signs and symptoms consistent with inhalation anthrax and a likelihood of exposure. This test is intended for use by military personnel, medical, and/or healthcare professionals only. The diagnosis of *B. anthracis* infection must be based on history, signs, symptoms, exposure likelihood, and additional laboratory evidence. A positive Active Anthrax Detect Plus Rapid Test result is presumptively diagnostic for *B. anthracis* infection. The definitive identification of *B. anthracis* from blood samples requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required. Testing should be performed and reported in accordance with current guidelines provided by the appropriate public health authorities. The level of lethal factor present in blood from individuals with early systemic infection is unknown. Negative results do not preclude infection with the biothreat microbial agents targeted by the device and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. This assay is for Rx use.

The distribution of *in vitro* diagnostic devices for *Bacillus* spp. detection is limited to laboratories that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities.

This assay is not FDA-cleared or approved for testing blood or plasma donors.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the Active Anthrax Detect Plus Rapid Test, and substantially equivalent devices of this generic type, into Class II under the generic name simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* spp. in human clinical samples.

FDA identifies this generic type of device as:

Simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* spp. in human clinical samples. A simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* species (spp.) is a prescription *in vitro* diagnostic device used to detect and presumptively identify *B. anthracis* and other *Bacillus* spp. in human clinical samples as an aid in the diagnosis of anthrax and other diseases caused by *Bacillus* spp. This device is simple to use and does not involve sample manipulation or measurement of an analyte that could be affected by conditions such as sample turbidity or cell lysis. This device may be used to aid in the presumptive diagnosis of anthrax in individuals who have signs and symptoms consistent with anthrax and a likelihood of exposure. *Bacillus* infections include anthrax (cutaneous, inhalational, or gastrointestinal) caused by *B. anthracis*, gastrointestinal disease, non-gastrointestinal infections, and an anthrax-like illness caused by *B. cereus*.

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 July 8, 2022, FDA received your De Novo requesting classification of the Active Anthrax Detect Plus Rapid Test. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the Active Anthrax Detect Plus Rapid 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 Active Anthrax Detect Plus Rapid 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:

Identified Risks to Health	Mitigation Measures
False positive/negative result	Certain limitations on distribution and sample collection Certain labeling information, including limitations, device descriptions, explanation of procedures and risk mitigations, and performance information Certain design verification and validation, including certain device description information and documentation of certain analytical studies and clinical studies
Exposure to test samples	Certain limitations on distribution and sample collection Certain labeling information, including device descriptions, explanation of procedures and risk mitigations, and performance information Certain design verification and validation, including certain device description information and documentation of certain analytical studies and clinical studies
Exposure to hazardous ingredients: • Hydrochloric acid ≤2.5% • Sodium azide 0.2%	Certain limitations on distribution and sample collection Certain labeling information, including device descriptions, explanation of procedures and risk mitigations, and performance information Certain design verification and validation, including certain device description information and documentation of certain analytical studies and clinical studies

In combination with the general controls of the FD&C Act, the simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* spp. in human clinical samples is subject to the following special controls:

1. The distribution of these devices is limited to laboratories that follow public health guidelines that address appropriate biosafety conditions, interpretation of test results, and coordination of findings with public health authorities.

2. Any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt (standalone or as part of a test system) for the collection of the sample types with which this device is intended to be used; alternatively, the sample collection device must be cleared in a premarket submission as a part of this device.

3. The labeling required under 21 CFR 809.10(b) must include:

    i. An intended use statement that includes the following:

        (A) A detailed description of targets the device detects and measures;

        (B) The results provided to the user (i.e., whether the measurement is qualitative, semi-quantitative, or quantitative);

        (C) The clinical indications appropriate for test use (e.g., in conjunction with patient history, epidemiological information, clinical observations, and other laboratory evidence to make patient management decisions);

        (D) Sample types with which it is intended for use;

        (E) The specific population(s) with which the device is intended to be used;

        (F) The testing location(s) where the device is to be used (if not intended for all locations);

        (G) A statement that the device results are for the presumptive identification of *Bacillus* spp., and definitive identification requires additional testing and confirmation procedures in consultation with the appropriate public health authorities;

        (H) A statement that negative results do not preclude infection with *Bacillus* spp. and should not be used as the sole basis for diagnosis, treatment, or other patient management decisions; and

        (I) A statement that testing is to be performed and reported in accordance with current guidelines provided by the appropriate public health authorities.

    ii. Detailed instructions for minimizing the risk of user exposure to *Bacillus* spp. that may be present in test samples and those used as control materials.

    iii. Detailed instructions for minimizing the risk of generating false positive test results due to contamination from positive test samples and/or positive control materials.

iv. A prominent and conspicuous precaution that interpretation of test results is intended to be performed by experienced healthcare professionals who have training in principles and use of infectious disease diagnostics and the expertise to report results.

v. A prominent and conspicuous warning statement that the test results alone do not conclusively establish infection and that additional testing and confirmation procedures may be necessary in consultation with the appropriate public health or other authorities to whom reporting is required.

vi. A detailed device description, including reagents, instruments, ancillary materials, all control elements, and a detailed explanation of the methodology, including all pre-analytical methods for processing of samples.

vii. Detailed descriptions of the performance characteristics of the device for all claimed sample types as shown by the analytical and clinical studies required under paragraphs (4)(ii) and (4)(iii), except sample stability performance characteristics.

viii. For any devices intended for use in a near-patient setting, a brief reference sheet for healthcare professionals that accompanies the device and that includes the name and intended use of the test, step-by-step instructions of all control and sample testing procedures for the claimed sample types, the result(s) interpretation, warning and limitation statements, and information for troubleshooting or technical assistance with the device.

ix. A statement that a nationally notifiable disease caused by a biothreat microbial agent must be reported to public health authorities in accordance with local, state, and federal law.

x. Limiting statements indicating, as applicable:

(A) Situations where the device has been demonstrated to fail or may not perform at its expected performance level (e.g., any disease specific circumstances or circumstances identified by human factors or robustness studies);

(B) Any specific circumstances that pose significant risk to public health, and for which the device has not been validated. For example:

a. Testing of matrices and patient populations that are not identified in the intended use; or
b. Testing individuals without signs and symptoms of infection, including mass infection screening (such as airport or border screening) that is not limited to individuals who have signs and symptoms and a risk of exposure to biothreat microbial agents.

4. Design verification and validation must include:

i. A detailed device description, including all device parts, control elements incorporated into the test procedure, reagents required but not provided, the principle of device operation and test

methodology, and the computational path from collected raw data to reported result (e.g., how collected raw signals are converted into a reported result).

ii. Detailed documentation of analytical studies, as applicable, including those demonstrating Limit of Detection (LoD), inclusivity, cross-reactivity, microbial interference, interfering substances, carryover/cross contamination, sample stability, within lab precision, hook effect, reproducibility, and other studies relevant to the technology (e.g., linearity), as determined to be appropriate by FDA.

iii. Detailed documentation and results from either a clinical study or, when determined to be acceptable by FDA, a study with an equivalent data set. Documentation from this study must include study reports, testing results, and results of all statistical analyses, including line data of all test samples, and an appropriate justification describing how the sample set is representative of the intended use population. This study must compare the device performance to results obtained from a reference or comparator method that FDA has determined to be appropriate. This study must include prospective (sequentially collected) samples for each intended sample type that are representative of the intended use populations and may, when determined to be acceptable by FDA, include additional characterized clinical samples; or, as an alternative, when determined to be acceptable by FDA, an equivalent sample set. This study must include samples spanning all relevant analyte concentrations for all of the indicated sample type(s) and the targeted analyte(s).

iv. A detailed description of the impact of any software, including software applications and hardware-based devices that incorporate software, on the device's functions, as applicable.

v. For any devices that detect the presence of an analyte directly from sample, detailed documentation and results from a shelf-life assessment that includes samples formulated in the most complex clinical matrix identified in the device's intended use.

vi. As part of the risk management activities, if the labeling includes hyperlinks to documents from public health authorities regarding sampling, sample shipment, sample testing, or clinical management of patients suspected of being infected; or if the labeling includes direct contact information for any such public health authority, then the hyperlinks and contact information must be reviewed at least annually and updated to reflect any changes to those hyperlinks or contact information.

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 simple *in vitro* diagnostic device for the detection of secreted proteins from *Bacillus* spp. in human clinical samples 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 Parts 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 Malik Raynor at malik.raynor@fda.hhs.gov.

Sincerely,

Uwe Scherf -S

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Director
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