September 29, 2022

Siemens Healthcare Diagnostics Products GmbH
Petra Dissmann
Regulatory Affairs Manager
Emil-von-Behring Strasse 76
Marburg, Hesse 35041
Germany

Re: DEN200067
Trade/Device Name: INNOVANCE VWF Ac
Regulation Number: 21 CFR 864.7293
Regulation Name: von Willebrand factor assay
Regulatory Class: Class II
Product Code: QTY
Dated: October 23, 2020
Received: October 28, 2020

Dear Petra Dissmann:

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 INNOVANCE VWF Ac, a prescription device with the following indications for use:

> In-vitro diagnostic automated assay for the quantitative determination of the von Willebrand factor-GPIb-binding activity in human plasma collected from venous blood samples in 3.2% sodium citrate tubes on the BCS XP System.
> As an aid used in the evaluation of patients with suspected or confirmed von Willebrand factor disorders.
> Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other laboratory findings.

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the INNOVANCE VWF Ac, and substantially equivalent devices of this generic type, into Class II under the generic name von Willebrand factor assay.

FDA identifies this generic type of device as:

> **von Willebrand factor assay.**: A von Willebrand factor assay is a prescription device intended for the measurement of von Willebrand factor activity or von Willebrand factor size distribution in human plasma. This device is indicated to aid in the diagnosis and management of patients being

evaluated for von Willebrand factor disorders in conjunction with other clinical and laboratory findings.

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 October 28, 2020, FDA received your De Novo requesting classification of the INNOVANCE VWF Ac. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the INNOVANCE VWF Ac 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 INNOVANCE VWF Ac 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
Falsely elevated von Willebrand factor (VWF) activity results may lead to delayed diagnosis and delayed patient management of von Willebrand disease (VWD). Patients with delayed diagnosis and resulting delayed patient management of VWD are at increased risk of bleeding due to the withholding of appropriate treatment.	Certain design verification and validation identified in special control (1), including documentation of certain analytical studies and clinical studies. Certain labeling information identified in special control (2), including limitations and performance information identified in special control (1).
Falsely depressed von Willebrand factor (VWF) activity results may lead the physician to suspect von Willebrand disease (VWD) in patients who do not have the disease. As a result, the patients may receive unnecessary follow-up testing and unnecessary treatment as well as delays in receiving a correct diagnosis and appropriate patient management. In	Certain design verification and validation identified in special control (1), including documentation of certain analytical studies and clinical studies. Certain labeling information identified in special control (2), including limitations and

Identified Risks to Health	Mitigation Measures
addition, affected patients may experience mental anxiety because of the erroneous diagnosis.	performance information identified in special control (1).
No results may lead to delayed patient management.	Certain design verification and validation identified in special control (1), including documentation of certain analytical studies and clinical studies. Certain labeling information identified in special control (2), including limitations and performance information identified in special control (1).

In combination with the general controls of the FD&C Act, the von Willebrand factor assay is subject to the following special controls:

1) Design verification and validation must include:

(i) Detailed documentation of studies demonstrating acceptable, as determined by FDA, analytical performance, including, as applicable, precision, linearity, assay interference, detection capability, specimen and reagent stability, and hook effect, with a sufficient number of specimens tested in order to obtain unbiased estimates of analytical performance. For devices measuring multiple analytes, the detailed documentation must include studies demonstrating the analytical performance of the device in regard to each individual analyte, including precision, linearity, assay interference, cross-reactivity, detection capability, specimen and reagent stability, and hook effect, as applicable.

(ii) Detailed documentation of a comparison study of clinical samples demonstrating performance relative to clinically relevant and appropriate, as determined by FDA, clinically validated laboratory tests. Further, the studies must meet all of the following criteria:

(A) All eligible subjects must meet appropriate study inclusion and exclusion criteria that define the intended use population. Specimens must be representative of the intended use population(s) and must representatively cover the full range of the device output and any clinically relevant decision points, as appropriate;

(B) The study must be conducted at a minimum of three external sites representative of the intended use setting by operators representative of the intended user population;

(C) For all intended pediatric patient populations, clinical outcome validation studies must study those populations in accordance with paragraph (1)(ii) (A) and (B);

(D) Expected (reference) values for test output must be demonstrated by testing a statistically appropriate number of samples from apparently healthy normal individuals in all relevant

subpopulations (i.e., blood group O and non-O, male and female, and, if applicable, pediatric and adults), as applicable to the intended use of the device.

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

(i) Limiting statements indicating, as applicable:

(A) This device should always be used in conjunction with the patient's medical history, clinical presentation, and other laboratory findings.

(B) Identification of any known interferents, including all endogenous, exogenous, technology-specific, and patient population-specific interferents, specific to the test outputs. The information must include the concentration(s) or level(s) of the interferent at which clinically significant interference was found to occur, and the concentration range or levels at which interference was not found to occur;

(ii) A detailed summary of the performance testing results of analytical and clinical performance testing, including results of concordance evaluation (overall agreement, positive percentage agreement and negative percentage agreement) as required under paragraph (1).

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 assay 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 Yan Cai at 240-402-1094.

Sincerely,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology and Hematology Devices
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