September 17, 2020

Instrumentation Laboratory Co.
Carol Marble
Regulatory Affairs Director
180 Hartwell Road
Bedford, Massachusetts 01730

Re: DEN190032
Trade/Device Name: HemosIL Liquid Anti-Xa
Regulation Number: 21 CFR 864.7295
Regulation Name: Heparin and direct oral factor Xa inhibitor drug test system
Regulatory Class: Class II
Product Code: QLU
Dated: June 24, 2019
Received: June 25, 2019

Dear Carol Marble:

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 HemosIL Liquid Anti-Xa, a prescription device with the following indications for use:

> HemosIL Liquid Anti-Xa is an automated chromogenic assay for in vitro diagnostic use by laboratory professionals in clinical laboratories. The assay provides quantitative results on 3.2% citrated human plasma for the following analytes based on the calibrators used:
>
> - When used with HemosIL Heparin Calibrators:
> Quantitative determination of unfractionated heparin (UFH) and low molecular weight heparin (LMWH) activity on the ACL TOP Family, ACL TOP Family 50 Series, and ACL Elite/Elite Pro.
>
> - When used with HemosIL Apixaban Calibrators:
> Quantitative determination of apixaban on the ACL TOP Family and ACL TOP Family 50 Series through measurement of Factor Xa activity, which is inversely proportional to the apixaban level. With HemosIL Apixaban Calibrators, the assay is intended to measure apixaban concentrations in patients on apixaban therapy in the following situations where measurement of apixaban levels could be useful to have as additional information:
> - Patients at risk for major bleeding
> - Patients experiencing a bleeding episode

The assay is not a stand-alone test and the results should be used in conjunction with other clinical and laboratory findings.

For use in adult population. For prescription use only.

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 HemosIL Liquid Anti-Xa, and substantially equivalent devices of this generic type, into Class II under the generic name Direct oral factor Xa inhibitor drug test system.

FDA identifies this generic type of device as:

Heparin and direct oral factor Xa inhibitor drug test system. A heparin and direct oral factor Xa inhibitor drug test system is intended for the detection of heparin and direct oral factor Xa inhibitors in human specimens collected from patients taking heparin or direct oral factor Xa inhibitors. This device is intended to aid in the management of therapy 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 June 25, 2019, FDA received your De Novo requesting classification of the HemosIL Liquid Anti-Xa. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the HemosIL Liquid Anti-Xa 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 HemosIL Liquid Anti-Xa 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 Risk	Mitigation Measures
False positive/false negative/failed to provide a result for diagnostics	Certain analytical studies and clinical studies in design verification and validation. Certain labeling information.

In combination with the general controls of the FD&C Act, the heparin and direct oral factor Xa inhibitor drug test system is subject to the following special controls:

(1) Design verification and validation must include the following:

(i) Detailed documentation of analytical device performance studies and results demonstrating acceptable analytical performance with a sufficient number of specimens tested in order to obtain unbiased estimates of analytical performance. This documentation shall include the following as appropriate to the technology, specimen types tested, and intended use of the device:

A. Studies and results for that demonstrate device precision including repeatability and reproducibility, using quality controls and clinical samples, when appropriate. Precision studies must assess specimens for each indicated drug at concentrations throughout the measuring range of the device including near clinically relevant levels, as appropriate. The study must evaluate different sources of variability including, as appropriate, between-run, between-operator, between-lot, between-instrument, between-day and between-site;

B. Studies and results that demonstrate that the device is free from clinically significant interference, from endogenous and exogenous interferents associated with the target population(s), and interferents that are specific for, or related to, the technology or methodology of the device;

C. Data to demonstrate appropriate specimen stability for the intended sample matrices under the intended conditions for specimen collection, handling, and storage described in the device labeling;

D. Studies and results that demonstrate the linear range, limit of blank (LoB), limit of detection (LoD), and limit of quantitation (LoQ), as applicable to the technology of the device;

E. For any devices intended for use for near patient testing, studies and results that demonstrate the robustness of the device in the hands of the intended user, including the entire testing procedure, pre-analytical specimen processing steps, and results interpretation.

(ii) Detailed documentation of clinical performance testing in which the performance is analyzed relative to a comparator that FDA has determined is appropriate. Specimens must be representative of the intended use population(s) and must cover the full range of the device output and any clinically relevant decision points as appropriate.

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

(i) 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 prominent statement that the device is not intended for use in monitoring patients taking heparin or direct oral factor Xa inhibitors;

(iii) Limiting statements indicating, as applicable:

(a) That the device should only be used in conjunction with information available from clinical evaluations and other diagnostic procedures;

(b) That the device is not specific to the direct oral factor Xa inhibitor that has been evaluated and may detect the presence of other direct factor Xa inhibitors that have not been evaluated.

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 Direct oral factor Xa inhibitor drug test system 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 Min Wu at 301-348-1886.

Sincerely,

Leonthena R. Carrington -S

Lea Carrington
Director
Division of Immunology and Hematology Devices
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and Radiological Health
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