October 4, 2022

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

Re: K213464
Trade/Device Name: HemosIL Liquid Anti-Xa
Regulation Number: 21 CFR 864.7525
Regulation Name: Heparin Assay
Regulatory Class: Class II
Product Code: KFF, QLU
Dated: June 3, 2022
Received: June 6, 2022

Dear Carol Marble:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 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 Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, 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).

Sincerely,

Min Wu
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name
HemosIL Liquid Anti-Xa

Indications for Use *(Describe)*

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 and ACL TOP Family 50 Series.

- 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Instrumentation Laboratory
A Werfen Company

510(k) Summary

This 510(k) Summary of Safety and Effectiveness is being submitted in accordance with the requirements of the Safe Medical Device Act of 1990 and 21 CFR 807.92.

Submitter's Information	Instrumentation Laboratory Company 180 Hartwell Road Bedford, MA 01730-2443 (USA)

Contact Person	Carol Marble Senior Director of Quality Assurance and Regulatory Affairs Phone: 781-861-4467 Fax: 781-861-4207 Email: cmarble@werfen.com

Preparation Date	June, 2022

Device Trade Name	HemosIL Liquid Anti-Xa

Predicate Device	HemosIL Liquid Anti-Xa	K090209, DEN190032

Regulatory Information					
Analyte	**Regulation Section**	**Regulatory Description**	**Class**	**Product Code**	**Panel**
Heparin	864.7525	Heparin Assay	II	KFF	81
Apixaban	864.7295	Anti-factor Xa Activity Test System, Apixaban	II	QLU	

Device Description
HemosIL Liquid Anti-Xa is a one stage chromogenic assay based on a synthetic chromogenic substrate and on Factor Xa inactivation. 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:** Heparin levels in patient plasma are measured automatically on ACL TOP Family and ACL TOP Family 50 Series when this assay is calibrated with HemosIL Heparin Calibrators. Heparin is analyzed as a complex with antithrombin present in the sample. The concentration of this complex is dependent on the availability of the patient's endogenous antithrombin. When the heparin-antithrombin complex is formed, two competing reactions take place. 1. Factor Xa is neutralized by heparin-antithrombin complex. 2. Residual Factor Xa is quantified with a synthetic chromogenic substrate. The paranitroaniline released is monitored kinetically at 405 nm and is inversely proportional to the heparin level in the sample. In order to reduce the influence from heparin antagonists, such as platelet factor 4 (PF4), dextran sulfate is included in the reaction mixture. • **When used with HemosIL Apixaban Calibrators:** Apixaban levels in patient plasma are measured automatically on ACL TOP Family and ACL TOP Family 50 Series when this assay is calibrated with HemosIL Apixaban Calibrators. Apixaban directly inhibits Factor Xa activity independent of the antithrombin present. The Factor Xa activity measured by the assay is exogenous. Factor Xa is neutralized directly by apixaban. Residual Factor Xa is quantified with a synthetic chromogenic substrate. The paranitroaniline released is monitored kinetically at 405 nm and is inversely proportional to the apixaban level in the sample. Measurement of apixaban concentration is recommended by the International Society of Thrombosis and Hemostasis Subcommittee on Control of Anticoagulation in certain clinical scenarios including bleeding episodes, perioperative management, and suspicion of overdose.

Indications for Use / Intended 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 and ACL TOP Family 50 Series.

- **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.

Reason for Submission

This Special 510(k) is being submitted to modify the labeled on-board instrument stability claims for HemosIL Liquid Anti-Xa on the ACL TOP Family and ACL TOP Family 50 Series from 7 days to 4 days for heparin and apixaban based on testing to the current CLSI EP25-A guideline. This submission also removes claims for heparin measurement on the ACL Elite/Elite Pro instrument family from the HemosIL Liquid Anti-Xa labeling.

The submission meets the criteria for a Special 510(k) based on the following:

- The proposed changes are submitted by the manufacturer legally authorized to market the existing device.
- There is a well-established method to evaluate the change: CLSI EP25-A.
- The data can be reviewed in a summary or risk analysis format.

In addition, the changes in this submission **do not** introduce:

- Changes to indications for use or intended use, ***except*** to remove the ACL Elite/Elite Pro instrument family
- Changes to operating principle
- Changes to formulation
- Changes to labeled performance claims, ***except*** to reduce the on-board instrument stability claims for the ACL TOP Family/ACL TOP Family 50 Series to 4 days for heparin and apixaban and to remove all claims for heparin measurement with the ACL Elite/Elite Pro instrument family

Comparison to Predicate		
Item	**Predicate Device [K090209 (heparin), DEN190032 (apixaban)]**	**Subject Device**
Similarities		
Trade Name	HemosIL Liquid Anti-Xa	Same
Manufacturer	Instrumentation Laboratory Company	Same
Intended Use/ Indications for Use **(Changes in Blue and Strikethrough)**	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~~,~~ and 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.	Same, ***except*** for removal of ACL Elite/Elite Pro instrument family

Comparison to Predicate			
Item	**Predicate Device [K090209 (heparin), DEN190032 (apixaban)]**		**Subject Device**
Similarities (Cont.)			
Test Principle	One stage chromogenic assay based on a synthetic chromogenic substrate and on factor Xa inactivation		Same
			Same
Sample Type	3.2% Citrated Plasma		Same
Measurement	Quantitative		Same
Reporting Units	Heparin	IU/mL	Same
	Apixaban	ng/mL	
Quality Control	Automated QC		Same
Limit of Detection	Heparin	0.04 IU/mL	Same
	Apixaban	9 ng/mL	
Linearity	Heparin	Up to 2 IU/mL	Same
	Apixaban	20 ng/mL – 1000 ng/mL	

Item	**Predicate Device [K090209 (heparin), DEN190032 (apixaban)]**	**Subject Device**
Differences		
Instrumentation	ACL TOP Family (K160276) ACL TOP Family 50 Series (K150877) ACL Elite/Elite Pro (K060162)	ACL TOP Family (K160276) ACL TOP Family 50 Series (K150877) **Note:** ACL Elite/Elite Pro claims removed
On-Board Stability	7 days at 15-25°C on the ACL TOP Family/ACL TOP Family 50 Series for heparin and apixaban	4 days at 15-25°C on the ACL TOP Family/ACL TOP Family 50 Series for heparin and apixaban

Conclusion	HemosIL Liquid Anti-Xa, with the modified claims for on-board instrument stability and the removal of claims for the ACL Elite/Elite Pro, is substantially equivalent to the legally marketed predicate device, HemosIL Liquid Anti-Xa, FDA cleared under K090209 for heparin measurement and FDA marketing authorized under DEN190032 for apixaban measurement.