January 28, 2025

Instrumentation Laboratory (IL) Co.
Nikita Malladi
Regulatory Affairs Manager II
180 Hartwell Rd
Bedford, Massachusetts 01730

Re: K243374
Trade/Device Name: HemosIL CL HIT-IgG$_{(PF4-H)}$
Regulation Number: 21 CFR 864.7695
Regulation Name: Platelet Factor 4 Radioimmunoassay
Regulatory Class: Class II
Product Code: LCO
Dated: October 30, 2024
Received: October 30, 2024

Dear Nikita Malladi:

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

YAN CAI-S

for
Min Wu, Ph.D.
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*

Device Name
HemosIL CL HIT-IgG(PF4-H)

Indications for Use *(Describe)*
HemosIL CL HIT-IgG(PF4-H) is a qualitative, fully automated, chemiluminescent immunoassay (CIA) for the detection of IgG antibodies that react with Platelet Factor 4 (PF4) when complexed to heparin. The assay is for use in human 3.2% citrated plasma on the ACL TOP 970 CL in a laboratory setting.
The result provided by the assay should be interpreted as either positive or negative based on the assay cut-off (1.00 U/mL). The positive or negative result aids in determining the risk for heparin induced thrombocytopenia (HIT) when used in conjunction with other laboratory and clinical findings.
Anti-PF4/Heparin antibodies are commonly found in patients with HIT. For use in adult population suspected of HIT. Not for use in isolation to exclude HIT.
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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510(k) Summary

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

510(k) Submitter	Instrumentation Laboratory (IL) Company 180 Hartwell Road Bedford, MA 01730-2443 (USA) Establishment Registration: 1217183	
Primary Contact	Nikita Malladi Regulatory Affairs Manager II Phone: 781-353-1486 Fax: 781-861-4207 Email: nmalladi@werfen.com	
Preparation Date	October 30, 2024	
Device Trade Name	HemosIL CL HIT-IgG$_{(PF4-H)}$	
Predicate Devices and 510(k) Number	HemosIL AcuStar HIT-IgG$_{(PF4-H)}$	K170854
Regulatory Information	**Chemiluminescent Assay**	
HemosIL CL HIT-IgG$_{(PF4-H)}$	Classification	Class II
	Classification Panel	Hematology (81)
	Regulation Section No.	21 CFR 864.7695
	Regulation Description	Platelet factor 4 radioimmunoassay
	Product Code	LCO

Chemiluminescent Assay	Device Description
HemosIL CL HIT IgG$_{(PF4-H)}$	HemosIL CL HIT-IgG$_{(PF4-H)}$ assay is a chemiluminescent two-step immunoassay consisting of magnetic particles coated with PF4 complexed to polyvinyl sulfonate (PVS) which capture, if present, PF4/H antibodies from the sample. After incubation, magnetic separation, and a wash step, a tracer consisting of an isoluminol-labeled anti-human IgG antibody is added and may bind with the captured PF4/H IgG on the particles. After a second incubation, magnetic separation, and a wash step, reagents that trigger the luminescent reaction are added, and the emitted light is measured as relative light units (RLUs) by the ACL TOP 970 CL optical system. The RLUs are directly proportional to the PF4/H IgG concentration in the sample. The HemosIL CL HIT-IgG$_{(PF4-H)}$ assay utilizes a 4 Parameter Logistic Curve fit (4PLC) data reduction method to generate a Master Curve. The Master Curve is predefined and lot dependent and it is stored in the instrument through the cartridge barcode. With the measurement of calibrators, the predefined Master Curve is transformed to a new, instrument specific 4PLC Working Curve. The concentration values of the calibrators are included in the reagent kit calibrator value sheet 2D barcode.
	Intended Use / Indication for Use
	HemosIL CL HIT-IgG$_{(PF4-H)}$ is a qualitative, fully automated, chemiluminescent immunoassay (CIA) for the detection of IgG antibodies that react with Platelet Factor 4 (PF4) when complexed to heparin. The assay is for use in human 3.2% citrated plasma on the ACL TOP 970 CL in a laboratory setting. The result provided by the assay should be interpreted as either positive or negative based on the assay cut-off (1.00 U/mL). The positive or negative result aids in determining the risk for heparin induced thrombocytopenia (HIT) when used in conjunction with other laboratory and clinical findings. Anti-PF4/heparin antibodies are commonly found in patients with HIT. For use with adult population suspected of HIT. Not for use in isolation to exclude HIT. For prescription use only.

HemosIL CL HIT-IgG(PF4-H) Comparison to Predicate Device		
Item	**Predicate Device (K170854)**	**New Device**
Trade Names	HemosIL AcuStar HIT-IgG(PF4-H)	HemosIL CL HIT-IgG(PF4-H)
Manufacturer	Instrumentation Laboratory Co.	Same
Measurand	Anti-PF4/Heparin IgG Antibodies	Same
Assay Type	Qualitative	Same
Product Code	LCO	Same
Regulation Section	21 CFR 864.7695	Same
Classification	Class II	Same
Intended Use	HemosIL AcuStar HIT-IgG(PF4-H) is a qualitative, fully automated, chemiluminescent immunoassay (CIA) for the detection of IgG antibodies that react with Platelet Factor 4 (PF4) when complexed to heparin. The assay is for use in human 3.2% or 3.8% citrated plasma and serum on the ACL AcuStar instrument in a laboratory setting. The result provided by the assay should be interpreted as either positive or negative based on the assay cut-off (1.00 U/mL). The positive or negative result aids in determining the risk for heparin induced thrombocytopenia (HIT) when used in conjunction with other laboratory and clinical findings. Anti-PF4/Heparin antibodies are commonly found in patients with HIT. For use in adult population suspected of HIT. Not for use in isolation to exclude HIT. For prescription use.	HemosIL CL HIT-IgG(PF4-H) is a qualitative, fully automated, chemiluminescent immunoassay (CIA) for the detection of IgG antibodies that react with Platelet Factor 4 (PF4) when complexed to heparin. The assay is for use in human 3.2% citrated plasma on the ACL TOP 970 CL in a laboratory setting. The result provided by the assay should be interpreted as either positive or negative based on the assay cut-off (1.00 U/mL). The positive or negative result aids in determining the risk for heparin induced thrombocytopenia (HIT) when used in conjunction with other laboratory and clinical findings. Anti-PF4/heparin antibodies are commonly found in patients with HIT. For use with adult population suspected of HIT. Not for use in isolation to exclude HIT. For prescription use only.

HemosIL CL HIT-IgG(PF4-H) Comparison to Predicate Device (Cont.)		
Item	**Predicate Device (K170854)**	**New Device**
Methodology	Chemiluminescent immunoassay (CIA)	Same
Reagents	Cartridge containing magnetic particle suspension coated with PF4 complexed to polyvinyl sulfonate (PVS)	Same
Antibodies	Mouse monoclonal anti-human IgG antibody	Same
Conjugate	Isoluminol conjugated anti-human IgG	Same
Cut-off	Fixed clinical cut-off: • Positive: ≥ 1.00 U/mL • Negative: < 1.00 U/mL	Same
Composition	1 cartridge containing 1 vial of magnetic particle suspension coated with PF4/PVS complex, 1 vial of assay buffer, 1 vial of tracer consisting of an mAb anti-human IgG antibody labeled with isoluminol, and 1 vial of sample diluent used for the regular predilution of the sample. The reagents are in a phosphate or Tris buffer containing bovine serum albumin, bovine fetal serum, PF4/PVS complex, mouse monoclonal IgG, stabilizers, and preservative.	1 cartridge containing 1 vial of magnetic particle suspension coated with PF4/PVS complex, 1 vial of assay buffer, 1 vial of tracer consisting of an mAb anti-human IgG antibody labeled with isoluminol, and 1 vial of sample diluent used for the regular predilution of the sample. The reagents are in a phosphate or HEPES buffer containing bovine serum albumin, bovine fetal serum, PF4/PVS complex, mouse monoclonal IgG, stabilizers, and preservative.
Calibrators	Two calibrator levels (included in the kit): • Calibrator 1 target value: 1.00 U/mL • Calibrator 2 target value: 16.00 U/mL Liquid format	Two calibrator levels (included in the kit): • Calibrator 1 target value: 1.00 U/mL • Calibrator 2 target value: 16.50 U/mL Liquid format
Controls	Two control levels (sold separately): • Low Control target value: 0.60 U/mL • High Control target value: 3.00 U/mL Liquid format	Two control levels (sold separately): • Low Control target value: 0.60 U/mL • High Control target value: 3.50 U/mL Liquid format
Sample Type	Human citrated plasma or serum	Human 3.2% citrated plasma
Instrumentation	ACL AcuStar	ACL TOP 970 CL

Performance Characteristics: New HemosIL CL Reagent			
Precision			
HemosIL CL HIT-IgG$_{(PF4-H)}$			
A precision study was performed in accordance with CLSI EP05-A3 (3rd Edition), using three lots of HemosIL CL HIT-IgG$_{(PF4-H)}$ reagent. Repeatability and within laboratory precision were assessed. To span the assay range, the study tested 5 plasma samples and 2 levels of HemosIL CL Multi-Ab Controls and 3 lots of HemosIL CL Multi-Ab Controls (low and high). Each material was run in duplicate, twice per day over 20 days on an ACL TOP 970 CL. The tables below show data for 1 representative reagent lot and also aggregated data for the 3 reagent lots.			
ACL TOP 970 CL	**Mean (U/mL)**	**Repeatability (% CV)**	**Within Laboratory (% CV)**
Low CL Multi-Ab Control	0.446	5.2	7.4
High CL Multi-Ab Control	3.231	3.0	5.9
Plasma Sample A (Pool)	0.248	8.2	10.7
Plasma Sample B (Pool)	0.907	2.9	5.7
Plasma Sample C (Pool)	1.346	3.1	6.5
Plasma Sample D (Unadulterated)	1.910	3.4	6.3
Plasma Sample E (Pool)	19.677	2.6	6.0

Performance Characteristics: New HemosIL CL Reagent (Cont.)		
Precision (Cont.)		
HemosIL CL HIT-IgG$_{(PF4-H)}$		
Aggregated data (Reagent Lots 1, 2, and 3)		
Material	**Mean (U/mL)**	**Lot-to-Lot Variability (% CV)**
Low CL Multi-Ab Control	0.440	2.1
High CL Multi-Ab Control	3.260	2.0
Plasma Sample A	0.272	8.1
Plasma Sample B	0.777	14.5
Plasma Sample C	1.210	9.7
Plasma Sample D	1.817	4.5
Plasma Sample E	21.451	9.5

Performance Characteristics: New HemosIL CL Reagent (Cont.)

Reproducibility

HemosIL CL HIT-IgG$_{(PF4-H)}$

Reproducibility studies were conducted at 3 external clinical sites using different operators (1 operator per site), on 3 different ACL TOP 970 CL systems (1 system per site), using 3 lots of HemosIL CL HIT-IgG$_{(PF4-H)}$. To span the assay range, the same 6 plasma samples were tested across the 3 sites, along with the HemosIL CL Multi-Ab Controls.

Each level for all materials was tested across 3 sites twice per day over 5 days with 3 replicates for each of the 3 reagent lots.

The pooled data for a representative reagent lot is presented below.

Level	Mean (U/mL)	N	Repeatability		Between-run		Between-day		Between-site		Between-lot		Reproducibility (Total)	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
Low CL Multi-Ab Control	0.515	270	0.0212	4.1	0.0241	4.7	0.0000	0.0	0.0195	3.8	0.0107	2.1	0.0390	7.6
High CL Multi-Ab Control	3.487	270	0.1047	3.0	0.1214	3.5	0.0530	1.5	0.0464	1.3	0.0803	2.3	0.1926	5.5
Plasma Sample 1 (Pool)	0.405	270	0.0521	12.9	0.0050	1.2	0.0098	2.4	0.0242	6.0	0.0000	0.0	0.0585	14.4
Plasma Sample 2 (Unadulterated)	0.050	270	All Replicates < 1.00 U/mL											
Plasma Sample 3 (Pool)	0.845	270	0.0509	6.0	0.0228	2.7	0.0255	3.0	0.0201	2.4	0.0000	0.0	0.0645	7.6
Plasma Sample 4 (Pool)	1.336	270	0.0813	6.1	0.0423	3.2	0.0000	0.0	0.0327	2.4	0.0250	1.9	0.1005	7.5
Plasma Sample 5 (Pool)	2.622	270	0.1015	3.9	0.0569	2.2	0.0505	1.9	0.0322	1.2	0.0960	3.7	0.1623	6.2
Plasma Sample 6 (Pool)	19.082	270	0.6650	3.5	0.4223	2.2	0.3153	1.7	0.8525	4.5	2.8821	15.1	3.1230	16.4

Performance Characteristics: New HemosIL CL Reagent (Cont.)
Analytical Sensitivity
Limit of detection (LoD) was assessed per CLSI EP17-A2 (2nd Edition) using three different lots of HemosIL CL HIT-IgG(PF4-H) reagent cartridges. Based on the results, the limit of blank (LoB) is 0.09 U/mL and the limit of detection (LoD) is 0.14 U/mL.
Linearity
Linearity was not applicable to this HemosIL CL HIT-IgG(PF4-H) submission.

Performance Characteristics: New HemosIL CL Reagent (Cont.)

Analytical Specificity

Interference testing was performed in accordance with CLSI EP07 (3rd Edition) using HemosIL CL HIT-IgG$_{(PF4-H)}$ reagent cartridge.

Based on the results, following are the interference claims for the new chemiluminescent assay:

No interference for:

• Hemoglobin	1000 mg/dL
• Bilirubin (unconjugated)	40 mg/dL
• Bilirubin (conjugated)	40 mg/dL
• Triglycerides	1500 mg/dL
• Unfractionated heparin	1.2 IU/mL
• Low molecular weight heparin	2.5 IU/mL
• Human anti-mouse antibodies (HAMA)	1 µg/mL
• Rheumatoid Factor	160 IU/mL
• Acid citric dextrose	0.45 g/dL
• Argatroban	1.2 µg/mL
• Fondaparinux	0.102 mg/dL
• Dabigatran	0.900 mg/dL
• Rivaroxaban	0.270 mg/dL
• Protamine	5 mg/dL

Twenty four citrated plasma samples from patients diagnosed with Antiphospholipid Syndrome (APS) were tested with the HemosIL CL HIT-IgG$_{(PF4-H)}$ assay and four commercially available antiphospholipid antibody assays (anti-cardiolipin IgG, anti-cardiolipin IgM, anti-β_2 glycoprotein I IgG, anti-β_2 glycoprotein I IgM). Three out of the twenty four samples recovered above the cut-off of 1.00 U/mL for HemosIL CL HIT-IgG$_{(PF4-H)}$. These three samples also tested positive for anti-cardiolipin IgG but tested negative for the other three antiphospholipid assays.

Performance Characteristics: New HemosIL CL Reagent (Cont.)

Normal Reference Range

A normal range study was performed in accordance with CLSI EP28-A3c (3rd Edition) using two lots of HemosIL CL HIT-IgG$_{(PF4)}$ reagent cartridge. The normal range was verified on the ACL TOP 970 CL. The threshold for positive HIT-IgG antibodies were established in the 90th percentile.

Cut-Off Validation: A method comparison with the Serotonin Release Assay (SRA) on 91 citrated plasma samples from HIT suspected patients (45 SRA positive and 46 SRA negative) validated a cut-off value of 1.00 U/mL (98.9% Agreement, 95% CI = 94.0% - 99.8%; 97.8% Negative Percent Agreement, 95% CI = 88.7% - 99.6%, 100.0% Positive Percent Agreement, 95% CI = 92.1% - 100.0%).

Following are the resultant upper limits of the normal range for the heparin exposed and healthy donors:

Reference Interval

Patient Population	No. of Citrated Plasma Samples	Upper Limit
Heparin Exposed, Non-HIT Suspected Patients	132	1.42 U/mL
Healthy Donors	122	0.45 U/mL

Based on these studies it has been determined that for heparin treated patient samples, HemosIL CL HIT-IgG$_{(PF4-H)}$ results equal to or higher than 1.00 U/mL may indicate the presence of anti-PF4/H antibodies.

Method Comparison

An external, multicenter method comparison study was performed at three clinical sites comparing HemosIL CL HIT-IgG$_{(PF4-H)}$ with HemosIL AcuStar HIT-IgG$_{(PF4-H)}$. The samples were from HIT-suspected patients. The results summarized below are based on a cut-off value of 1.00 U/mL for the HemosIL CL HIT-IgG$_{(PF4-H)}$ assay and the HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ assay.

		HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ Results		
		+	-	Total
HemosIL CL HIT-IgG$_{(PF4-H)}$ Results	+	91	1	92
	-	3	246	249
	Total	94	247	341
		Proportion	Wilson 95% CI	
PPA (Positive Percent Agreement)		97% (91/94)	91%	99%
NPA (Negative Percent Agreement)		100% (246/247)	98%	100%
Total Percent Agreement		99% (337/341)	97%	100%

Conclusion
Based on the substantial equivalence comparison and the results of the conducted performance evaluations, the HemosIL CL HIT-IgG$_{(PF4-H)}$ assay on the ACL TOP 970 CL was shown to be substantially equivalent to the cleared and currently marketed device, HemosIL AcuStar HIT-IgG$_{(PF4-H)}$ (K170854) on the ACL AcuStar (K083518). The differences between the subject and predicate devices do not impact safety and effectiveness.