September 29, 2023

Instrumentation Laboratory Co.
Nikita Malladi
Principal Regulatory Affairs Specialist
180 Hartwell Road
Bedford, Massachusetts 01730

Re: K221359
Trade/Device Name: ACL TOP 970 CL, HemosIL CL Anti-Cardiolipin IgM, HemosIL CL Anti-ß2 Glycoprotein-I IgM
Regulation Number: 21 CFR 864.5425
Regulation Name: Multipurpose System For In Vitro Coagulation Studies
Regulatory Class: Class II
Product Code: JPA, MID, MSV
Dated: May 10, 2022
Received: May 11, 2022

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.

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,

Min Wu -S

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K221359

Device Name
ACL TOP 970 CL, HemosIL CL Anti-Cardiolipin IgM and HemosIL CL Anti-ß2 Glycoprotein-I IgM

Indications for Use *(Describe)*

ACL TOP 970 CL
The ACL TOP 970 CL is a bench top, fully automated, random access analyzer designed specifically for in vitro diagnostic use by health care professionals in a clinical laboratory.
The system provides results for both direct measurements and calculated parameters.

HemosIL CL Anti-Cardiolipin IgM
HemosIL CL Anti-Cardiolipin IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings.
For use with adult population. For prescription use only.

HemosIL CL Anti-ß2 Glycoprotein-I IgM
HemosIL CL Anti-ß2 Glycoprotein-I IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-ß2 Glycoprotein-I (anti-ß2GPI) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings.
For use with 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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510(k) Summary

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

Submitter's Information	Instrumentation Laboratory (IL) Co. 180 Hartwell Road Bedford, MA 01730, USA
Contact 1 (Primary)	Nikita Malladi, Regulatory Affairs Manager I Phone: 781-353-1486 Fax: 781-861-4207 Email: nmalladi@werfen.com
Preparation Date	September 28, 2023

Device Trade Names	ACL TOP 970 CL
	HemosIL CL Anti-Cardiolipin IgM
	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM

Predicate Devices and 510(k) Numbers	**Instrument**	ACL AcuStar	K083518
	Assays	HemosIL AcuStar Anti-Cardiolipin IgM	K092181
		HemosIL AcuStar Anti-β_2 Glycoprotein-I IgM	K091556

Regulatory Information		
ACL TOP 970 CL	**Instrument**	
	Regulation Section No.	21 CFR 864.5425
	Regulation Description	Multipurpose system for *in vitro* coagulation studies
	Classification	Class II
	Product Code	JPA
	Panel	Hematology (81)
HemosIL CL Anti-Cardiolipin IgM	**Chemiluminescent Assays**	
	Regulation Section No.	21 CFR 866.5660
	Regulation Description	System, Test, Anti-cardiolipin Immunological
	Classification	Class II
	Product Code	MID
	Panel	Immunology (82)
HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM	Regulation Section No.	21 CFR 866.5660
	Regulation Description	System, Test, Antibodies, β_2 - Glycoprotein I (β_2 - Gpi)
	Classification	Class II
	Product Code	MSV
	Panel	Immunology (82)

Reasons for Submission
This Traditional 510(k) is submitted by Instrumentation Laboratory Co. for the following reasons: • To obtain FDA clearance for the ACL TOP 970 CL instrument • To obtain FDA clearance for two new immunoassays (HemosIL CL Anti-Cardiolipin IgM and HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM)

Device Description	
Instrument	
ACL TOP 970 CL Instrument	The ACL TOP 970 CL is an instrument that integrates new chemiluminescent test capability similar to the ACL AcuStar, K083518.
Chemiluminescent Assays	
HemosIL CL Anti-Cardiolipin IgM	HemosIL CL Anti-Cardiolipin IgM is a chemiluminescent two-step immunoassay consisting of magnetic particles coated with cardiolipin and human purified ß$_2$GPI, which capture, if present, the aCL antibodies from the sample. After incubation, magnetic separation, and a wash step, a tracer consisting of an isoluminol-labeled anti-human IgM antibody is added and may bind with the captured aCL IgM on the particles. After a second incubation, magnetic separation, and wash step, reagents that trigger the luminescent reaction are added, and the emitted light is measured as relative light units (RLU) by the ACL TOP 970 CL optical system. RLUs are directly proportional to the aCL IgM concentration in the sample.
HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM is a chemiluminescent two-step immunoassay consisting of magnetic particles coated with human purified ß$_2$GPI, which capture, if present, the aß$_2$GPI antibodies from the sample. After incubation, magnetic separation, and a wash step, a tracer consisting of an isoluminol-labeled anti-human IgM antibody is added and may bind with the captured aß$_2$GPI IgM on the particles. After a second incubation, magnetic separation, and 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. RLUs are directly proportional to the aß$_2$GPI IgM concentration in the sample.

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Intended Use / Indications for Use	
Instrument	
ACL TOP 970 CL	The ACL TOP 970 CL is a bench top, fully automated, random access analyzer designed specifically for in vitro diagnostic use by health care professionals in a clinical laboratory. The system provides results for both direct measurements and calculated parameters.
Chemiluminescent Assays	
HemosIL CL Anti-Cardiolipin IgM	HemosIL CL Anti-Cardiolipin IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP® 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings. For use with adult population. For prescription use only.
HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-ß$_2$ Glycoprotein-I (anti-ß$_2$GPI) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP® 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings. For use with adult population. For prescription use only.

ACL TOP 970 CL Instrument Comparison to Predicate Device		
Item	**Predicate Device No.: K083518**	**Subject Device**
Trade Names	ACL AcuStar	ACL TOP 970 CL
Intended Use/ Indications for Use	The ACL AcuStar is an automated immunoassay analyzer designed specifically for *in vitro* diagnostic use in a clinical laboratory. The assay analysis is based on chemiluminescent technology. The system provides results for both direct measurements and calculated parameters.	The ACL TOP 970 CL is a bench top, fully automated, random access analyzer designed specifically for *in vitro* diagnostic use by health care professionals in a clinical laboratory. The system provides results for both direct measurements and calculated parameters.
Quality Control	Automated QC	Automated QC
Methodology	Chemiluminescence reading unit and photo multiplier tube (PMT)	Similar chemiluminescence reading unit and Photo Multiplier Tube (PMT) to the ACL AcuStar.
Interface	Windows 7 Operating System	Windows 10 Operating System

HemosIL CL Anti-Cardiolipin IgM Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, HemosIL CL Anti-Cardiolipin IgM, and its predicate device, the currently marketed HemosIL AcuStar Anti-Cardiolipin IgM (K092181).		
Item	**Predicate Device: K092181**	**Subject Device**
Trade Name	HemosIL AcuStar Anti-Cardiolipin IgM	HemosIL CL Anti-Cardiolipin IgM
Intended Use/ Indications for Use	HemosIL AcuStar Anti-Cardiolipin IgM is a fully automated chemiluminescent assay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgM antibodies in human citrated plasma and serum on the ACL AcuStar, as an aid in the diagnosis of thrombotic disorders related to primary and secondary Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings.	HemosIL CL Anti-Cardiolipin IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP® 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings. For use with adult population. For prescription use only.
Type of Test	Semi-quantitative	Same
Technology	Two-step chemiluminescent immunoassay	Same
Clinical Cut-off	20.0 U/mL	Same
Calibrator	Calibrator 1: 1 x 1 mL barcoded tube of a solution with aCL IgM in saline solution containing bovine fetal serum, stabilizers, and preservative. Calibrator 2: 1 x 1 mL barcoded tube of a solution with aCL IgM in saline solution containing bovine fetal serum, stabilizers, and preservative.	Calibrator 1: 1 x 1.2 mL barcoded vial of a solution with aCL IgM in saline solution containing bovine fetal serum, stabilizers, and preservative. Calibrator 2: 1 x 1.2 mL barcoded vial of a solution with aCL IgM in saline solution containing bovine fetal serum, stabilizers, and preservative.
Composition	1 cartridge containing 1 vial of magnetic particle suspension coated with bovine cardiolipin and human purified β_2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgM antibody labeled with isoluminol, and 1 vial of sample diluent used for the regular predilution of the sample and automated dilution in the rerun. The reagents are in a phosphate or borate buffer containing bovine serum albumin, bovine cardiolipin, human β_2GPI, mouse monoclonal IgM, stabilizers, and preservative.	1 cartridge containing 1 vial of magnetic particle suspension coated with bovine cardiolipin and human purified ß$_2$GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgM antibody labeled with isoluminol, and 1 vial of sample diluent. The reagents are in a phosphate or borate buffer containing bovine serum albumin, bovine cardiolipin, human ß$_2$GPI, mouse monoclonal IgM, stabilizers, and preservative.

HemosIL CL Anti-Cardiolipin IgM Comparison to Predicate Device (Cont.)		
Item	**Predicate Device: K092181**	**Subject Device**
Trade Name	HemosIL AcuStar Anti-Cardiolipin IgM	HemosIL CL Anti-Cardiolipin IgM
Sample Type	Serum or Citrated Plasma	Human 3.2% or 3.8% citrated plasma
Quality Control	Low and high controls (sold separately)	Different control material, with two levels at or near cut-off and at abnormal level
Detection Limit	1.0 U/mL	2.0 U/mL
Linearity	1.0 – 774 U/mL	2.7 – 500.0 U/mL
	When the rerun capability of the instrument is activated, the instrument makes an automatic dilution and corrects the final result for the dilution factor (20x), thereby expanding the test range to 15,480 U/mL.	The assay is not affected by prozone effect. The assay protocol has a washing step after the sample incubation that precludes the prozone effect.

HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM, and its predicate device, the currently marketed HemosIL AcuStar Anti-β$_2$ Glycoprotein-I IgM (K091556).		
Item	**Predicate Device: K091556**	**Subject Device**
Trade Name	HemosIL AcuStar Anti-β$_2$ Glycoprotein-I IgM	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM
Intended Use/ Indications for Use	HemosIL AcuStar Anti-β$_2$ Glycoprotein-I IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-β$_2$ Glycoprotein-I (anti-β$_2$GPI) IgM antibodies in human citrated plasma and serum on the ACL AcuStar, as an aid in the diagnosis of thrombotic disorders related to primary and secondary Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings.	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM is a fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-ß$_2$ Glycoprotein-I (anti-ß$_2$GPI) IgM antibodies in human 3.2% or 3.8% citrated plasma on the ACL TOP® 970 CL in the laboratory setting by a healthcare professional, as an aid in the diagnosis of Antiphospholipid Syndrome (APS) when used in conjunction with other laboratory and clinical findings. For use with adult population. For prescription use only.
Type of Test	Semi-quantitative	Same
Technology	Two-step chemiluminescent immunoassay	Same
Clinical Cut-off	20.0 U/mL	Same
Calibrator	Calibrator 1: 1 x 1 mL barcoded tube of a solution with aß$_2$GPI IgM in a phosphate buffer containing bovine serum albumin, stabilizers, and preservative. Calibrator 2: 1 x 1 mL barcoded tube of a solution with aß$_2$GPI IgM in a phosphate buffer containing bovine serum albumin, stabilizers, and preservative.	Calibrator 1: 1 x 1.2 mL barcoded vial of a solution with aß$_2$GPI IgM in a phosphate buffer containing bovine serum albumin, stabilizers, and preservative. Calibrator 2: 1 x 1.2 mL barcoded vial of a solution with aß$_2$GPI IgM in a phosphate buffer containing bovine serum albumin, stabilizers, and preservative.
Composition	1 cartridge containing 1 vial of a magnetic particle suspension coated with human purified ß$_2$GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgM antibody labeled with isoluminol, and 1 vial of sample diluent used for the regular predilution of the sample and automatic dilution in rerun. The reagents are in a phosphate buffer containing bovine serum albumin, human ß$_2$GPI, mouse monoclonal IgM, stabilizers, and preservative.	1 cartridge containing 1 vial of a magnetic particle suspension coated with human purified ß$_2$GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgM antibody labeled with isoluminol, and 1 vial of sample diluent. The reagents are in a phosphate buffer containing bovine serum albumin, human ß$_2$GPI, mouse monoclonal IgM, stabilizers, and preservative.

HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM Comparison to Predicate Device (Cont.)		
Item	**Predicate Device: K091556**	**Subject Device**
Trade Name	HemosIL AcuStar Anti-β_2 Glycoprotein-I IgM	HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM
Sample Type	Serum or Citrated Plasma	Human 3.2% or 3.8% citrated plasma
Quality Control	Low and high controls (sold separately)	Different control material with two levels at or near cut-off and at abnormal level
Detection Limit	1.1 U/mL	1.0 U/mL
Linearity	1.1 – 841 U/mL	1.9 – 400.0 U/mL
	When the rerun capability of the instrument is activated, the instrument makes an automatic dilution and corrects the final result for the dilution factor (20x), thereby expanding the test range to 16,820 U/mL.	The assay is not affected by prozone effect. The assay protocol has a washing step after the sample incubation that precludes the prozone effect.

Performance Characteristics: New HemosIL CL Reagents
Precision
HemosIL CL Anti-Cardiolipin IgM
A precision study was performed in accordance with CLSI EP05-A3 (3rd Edition), using three lots of HemosIL CL Anti-Cardiolipin IgM reagents. Repeatability and within laboratory precision were assessed. To span the assay range, the study tested 5 plasma samples (3 positive; 2 negative), 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 table below shows the aggregated data for the 3 reagent lots.

Material	**Mean (U/mL)**	**Lot-to-Lot Variability (% CV)**
Low Multi-Ab Control	8.4	1.6
High Multi-Ab Control	86.1	1.2
Plasma Sample A	5.5	9.6
Plasma Sample B	15.7	5.2
Plasma Sample C	24.3	2.7
Plasma Sample D	107.5	1.6
Plasma Sample E	396.4	2.3

Performance Characteristics: New HemosIL CL Reagents (Cont.)
Precision (Cont.)
HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM
A precision study was performed in accordance with CLSI EP05-A3 (3rd Edition), using three lots of HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagents. Repeatability and within laboratory precision were assessed. To span the assay range, the study tested 5 plasma samples (3 positive; 2 negative), 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 table below shows aggregated data for the 3 reagent lots.

Material	Mean (U/mL)	Lot-to-Lot Variability (% CV)
Low Multi-Ab Control	4.1	12.8
High Multi-Ab Control	51.5	11.5
Plasma Sample A	8.4	5.6
Plasma Sample B	15.0	4.4
Plasma Sample C	21.7	3.6
Plasma Sample D	96.9	7.2
Plasma Sample E	297.3	7.1

Performance Characteristics: New HemosIL CL Reagents (Cont.)

Reproducibility

HemosIL CL Anti-Cardiolipin IgM

Reproducibility studies were conducted at 3 external sites, in accordance with CLSI EP05-A3 (3rd Edition), 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 Anti-Cardiolipin IgM and 1 lot of HemosIL CL Multi-Ab Controls. To span the assay range, 4 plasma samples (3 positive and 1 negative) were also tested across the 3 sites.

Each material was tested in triplicate, twice a day for 5 days, for a total of 30 replicates per level.

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

Level	Mean (U/mL)	N	Repeatability		Between-run		Between-day		Between-site		Reproducibility	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
Low Multi-Ab Control	8.6	90	0.40	4.6	0.28	3.3	0.00	0.0	0.36	4.2	0.61	7.0
High Multi-Ab Control	100.3	90	3.86	3.8	5.24	5.2	0.00	0.0	3.47	3.5	7.37	7.4
Clinical Sample 1 (pool)	5.5	90	0.22	3.9	0.38	6.9	0.16	2.9	0.24	4.4	0.52	9.5
Clinical Sample 2 (pool)	30.0	90	1.01	3.4	0.70	2.3	0.00	0.0	0.58	1.9	1.36	4.5
Clinical Sample 3 (unadultera ted)	97.7	90	4.49	4.6	2.82	2.9	0.00	0.0	3.67	3.8	6.45	6.6
Clinical Sample 4 (pool)	402.9	90	12.42	3.1	24.89	6.2	10.12	2.5	9.47	2.3	31.08	7.7

Performance Characteristics: New HemosIL CL Reagents (Cont.)

Reproducibility (Cont.)

HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM

Reproducibility studies were conducted at 3 external sites, in accordance with CLSI EP05-A3 (3rd Edition), 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 Anti-ß$_2$ Glycoprotein-I IgM and 1 lot of HemosIL CL Multi-Ab Low and High Controls. To span the assay range, 4 plasma samples (3 positive and 1 negative) were also tested across the 3 sites.

Each material was tested in triplicate, twice a day for 5 days, for a total of 30 replicates per level.

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

Level	Mean (U/ML)	N	Repeatability		Between-run		Between-day		Between-site		Reproducibility	
			SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
Low Multi-Ab Control	9.9	90	0.42	4.2	0.58	5.9	0.00	0.0	0.40	4.1	0.82	8.3
High Multi-Ab Control	125.3	90	4.72	3.8	6.45	5.1	0.00	0.0	5.36	4.3	9.62	7.7
Clinical Sample 1 (pool)	8.5	90	0.24	2.8	0.41	4.8	0.00	0.0	0.52	6.1	0.71	8.3
Clinical Sample 2 (pool)	27.9	90	0.70	2.5	0.78	2.8	0.37	1.3	1.20	4.3	1.64	5.9
Clinical Sample 3 (unadulterated)	94.4	90	2.57	2.7	3.12	3.3	1.59	1.7	4.98	5.3	6.61	7.0
Clinical Sample 4 (unadulterated)	288.1	90	5.65	2.0	8.93	3.1	3.76	1.3	8.16	2.8	13.87	4.8

Performance Characteristics: New HemosIL CL Reagents (Cont.)

Analytical Sensitivity

Limit of detection (LoD) was assessed per CLSI EP17-A2 (2nd Edition) using three different lots of HemosIL CL Anti-Cardiolipin IgM and three different lots of HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagent cartridges. LoD samples were prepared by combining Ab-positive donor plasma and normal donor plasma per protocol. Based on the results, following are the limits of detection (LoDs) for the two assays:

HemosIL CL Anti-Cardiolipin IgM		**HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM**	
LoD	2.0 U/mL	LoD	1.0 U/mL
LoQ	2.0 U/mL	LoQ	1.0 U/mL

Linearity

Linearity was assessed per CLSI EP06 (2nd Edition) using three different lots of HemosIL CL Anti-Cardiolipin IgM and three different lots of HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagent cartridges. For each assay, a set of linearity samples were prepared by diluting a high antibody plasma sample with a negative antibody plasma sample to create the required sample concentrations. Each level was measured in seven replicates with the three lots for each assay. The linearity range was determined such that all acceptance criteria were met.

Based on the results, following are the linear ranges for the two assays:

HemosIL CL Anti-Cardiolipin IgM		**HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM**	
Linearity Range	2.7 - 500.0 U/mL	Linearity Range	1.9 - 400.0 U/mL
The assay is not affected by prozone effect. The assay protocol has a washing step after the sample incubation that precludes the prozone effect.		The assay is not affected by prozone effect. The assay protocol has a washing step after the sample incubation that precludes the prozone effect.	

Performance Characteristics: New HemosIL CL Reagents (Cont.)	
Analytical Specificity	
Interference testing was performed in accordance with CLSI EP07 (3rd Edition) using HemosIL CL Anti-Cardiolipin IgM and HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagent cartridges. Based on the results, following are the interference claims for the two assays:	
HemosIL CL Anti-Cardiolipin IgM	**HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM**
No interference for: • Hemoglobin up to 1000 mg/dL • Bilirubin up to 40 mg/dL • Triglycerides up to 1500 mg/dL • Heparin (LMW and UF) up to 3.3 IU/mL • Rheumatoid Factor up to 500 IU/mL • Acetylsalicylic acid up to 3 mg/dL • Atorvastatin up to 0.075 mg/dL • Warfarin up to 7.5 mg/dL • Prednisone up to 9.90E-03 mg/dL • Acid Citric Dextrose up to 4.5 g/dL • Hydroxychloroquine up to 777.6 ng/mL • Rituximab up to 318 mcg/mL	No interference for: • Hemoglobin up to 1000 mg/dL • Bilirubin up to 40 mg/dL • Triglycerides up to 1500 mg/dL • Heparin (LMW and UF) up to 3.3 IU/mL • Rheumatoid Factor up to 500 IU/mL • Acetylsalicylic acid up to 3 mg/dL • Atorvastatin up to 0.075 mg/dL • Warfarin up to 7.5 mg/dL • Prednisone up to 9.90E-03 mg/dL • Acid Citric Dextrose up to 4.5 g/dL • Hydroxychloroquine up to 777.6 ng/mL • Rituximab up to 318 mcg/mL
The possible interference of cryoglobulins should be considered in the interpretation of the results.[1]	

1. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006; 4: 295-306.

Performance Characteristics: New HemosIL CL Reagents (Cont.)

Normal Reference Range

A normal range study was performed in accordance with CLSI EP28-A3c (3rd Edition) using one lot of HemosIL CL Anti-Cardiolipin IgM and one lot of HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagent cartridges. The normal range was verified on the ACL TOP 970 CL using 100 citrated plasma normal donor samples. The threshold for positive aCL IgM and positive aß$_2$GPI IgM antibodies were established in the 99th percentile.

Following are the resultant upper limits of the normal range for the two assays:

HemosIL CL Anti-Cardiolipin IgM		**HemosIL CL Anti- ß$_2$ Glycoprotein-I IgM**	
Upper Limit	20.0 U/mL	Upper Limit	20.0 U/mL

Due to many variables which may impact results, each laboratory should determine its own normal range.

Method Comparison

A method comparison study was performed, comparing the performance of HemosIL CL Anti-Cardiolipin IgM and HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM reagent cartridges with the respective predicate devices.

HemosIL CL Anti-Cardiolipin IgM

A method comparison was performed comparing HemosIL CL Anti-Cardiolipin IgM with a commercially available chemiluminescence assay.

System	**N**	**Slope (95% CI)**	**r**	**Reference Method**
ACL TOP 970 CL	131	1.00 (0.98 – 1.01)	1.00	ACL AcuStar

HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM

A method comparison was performed comparing HemosIL CL Anti-ß$_2$ Glycoprotein-l IgM with a commercially available chemiluminescence assay.

System	**N**	**Slope (95% CI)**	**r**	**Reference Method**
ACL TOP 970 CL	123	0.94 (0.92 – 0.96)	0.99	ACL AcuStar

Performance Characteristics: New HemosIL CL Reagents (Cont.)

APS Outcome Study

HemosIL CL Anti-Cardiolipin IgM

A diagnostic clinical performance study was performed comparing HemosIL CL Anti-Cardiolipin IgM with APS disease classification per 2006 International Consensus Statement from Miyakis et al.[1]

	APS Classification	
HemosIL CL Anti-Cardiolipin IgM	**Positive**	**Negative**
Positive	77	25
Negative	113	285

Predicate Device	**N**	**Sensitivity (95% CI)**	**Specificity (95% CI)**
APS Classification	500	40.5% (33.8% - 47.6%)	91.9% (88.4% - 94.5%)

HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM

A diagnostic clinical performance study was performed comparing HemosIL CL Anti-ß$_2$ Glycoprotein-l IgM with APS disease classification per 2006 International Consensus Statement from Miyakis et al.[1]

	APS Classification	
HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM	**Positive**	**Negative**
Positive	63	17
Negative	128	295

Predicate Device	**N**	**Sensitivity (95% CI)**	**Specificity (95% CI)**
APS Classification	503	33.0% (26.7% - 39.9%)	94.6% (91.4% - 96.6%)

1. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost. 2006; 4: 295-306.

Conclusion
Based on the substantial equivalence comparison and the results of the conducted performance evaluations, the HemosIL CL Anti-Cardiolipin IgM and the HemosIL CL Anti-ß$_2$ Glycoprotein-I IgM assays on the ACL TOP 970 CL were shown to be substantially equivalent to the cleared and currently marketed devices, HemosIL AcuStar Anti-Cardiolipin IgM (K092181) and HemosIL AcuStar Anti-β_2 Glycoprotein-I IgM assays (K091556) on the ACL AcuStar (K083518). The differences between the subject and predicate devices do not impact safety and effectiveness.