February 6, 2026

Inova Diagnostics, inc.
Edward Brehm
Staff Regulatory Affairs Specialist
9900 Old Grove Rd
San Diego, California 92131

Re: K243979
Trade/Device Name: Aptiva APS IgA Reagent
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: Class II
Product Code: MSV, MID
Dated: December 23, 2025
Received: December 23, 2025

Dear Edward Brehm:

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,

Ying Mao -S

Ying Mao, 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)*
K243979

Device Name
Aptiva APS IgA Reagent

Indications for Use *(Describe)*
The Aptiva APS IgA Reagent is an immunoassay utilizing particle-based multi-analyte technology for the semi-quantitative determination of anti-cardiolipin (aCL) and anti-beta 2 glycoprotein 1 (aβ2GPI) IgA autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory and clinical findings.

The Aptiva APS IgA Reagent is intended for use with the Aptiva System.

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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"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Table of Contents

This summary of the 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Administrative data

Submitter: Inova Diagnostics, Inc
9900 Old Grove Road,
San Diego, CA, 92131

Date Prepared: 01/29/2026

Purpose of submission: New device

Device in the submission: Aptiva APS IgA Reagent

Primary Contact:
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9900 Old Grove Road, San Diego, CA, 92131
Email: ebrehm@werfen.com

Device name (kit):

Proprietary name:	Aptiva APS IgA Reagent
Common name:	anti-cardiolipin antibody immunoassay, anti-beta2-glycprotein1 immunoassay
Classification name:	System, Test, Anticardiolipin Immunological System, Test, Beta2 Glycoprotein1 Immunological

Regulation Description	Multiple autoantibodies immunological test system
Regulation Medical Specialty	Immunology
Review Panel	Immunology
Product Code	Anticardiolipin: MID B2 – Glycoprotein I: MSV
Regulation Number	866.5660
Device Class	2

Predicate device

QUANTA Flash® aCL IgA, 510(k) number: K120817
QUANTA Flash® β2GP1 IgA, 510(k) number: K120817

Device description

The Aptiva APS IgA reagent utilize particle based multi-analyte technology (PMAT) in a cartridge format. Each analyte (anti-cardiolipin [aCL] and anti-β2-Glycoprotein I [aβ2GPI]) in the Aptiva APS IgA reagent is a solid phase immunoassay utilizing fluorescent microparticles. This technology allows each of the two analytes, along with a human IgA capture antibody (IgA Control Microparticle), to be coated onto three uniquely recognizable paramagnetic microparticles, which are combined into one tube.

The Aptiva instrument is a fully automated, random-access analyzer. This platform is a closed system with continuous load and random-access capabilities that processes the samples, runs the reagent and reports results. It includes liquid handling hardware, optical module (OM), and integrated computer with proprietary software and touch screen user interface.

The two analyte microparticles, along with the control microparticle, are stored in the reagent cartridge under conditions that preserve the proteins in their reactive states. When the assay cartridge is ready to be used for the first time, the reagent tube seals are pierced using the cartridge lid. The reagent cartridge is then loaded onto the Aptiva instrument, where the microparticles are automatically rehydrated using a buffer located within the cartridge.

The Aptiva System dilutes the sample 1:8, then combines an aliquot of diluted sample, and reagent into a cuvette. The mixture is incubated at 37°C. After a wash cycle, conjugated anti-human IgG or IgM antibodies are added to the particles and this mixture is incubated at 37°C. Excess conjugate is removed in another wash cycle, and the particles are re-suspended in system fluid.

Multiple images are generated by the system to identify and count the two (2) unique analyte particles, as well as determine the amount of conjugate on each particle. A third particle, coated with goat anti-human IgA antibodies, is present in the reagent as a control to flag low concentrations of IgA in the sample as an assay verification step. The median fluorescent intensity (MFI) for each analyte is proportional to the concentration of conjugate bound to human IgA, which is proportional to the concentration of IgA antibodies bound to the corresponding particle population. The system uses the MFI from at least 50 particles of each population. The identity of the particles is determined by the unique signature of the particles.

Each analyte in the Aptiva APS IgA Reagent is assigned a predefined lot specific master curve. The analyte specific master curve is stored on the reagent cartridge RFID label. Based on results obtained by running calibrators (supplied separately), the system creates individual working curves. Working curves are used by the software to calculate Fluorescent Light Units (FLU) for each analyte from the MFI values obtained for each sample.

Aptiva APS IgA Calibrators and Aptiva APS IgA Controls are sold separately.

The Aptiva APS IgA Reagent kit contains the following materials:

Contents	Active Ingredient	Quantity	Symbol
1. Aptiva APS IgA Reagent Cartridge	-	1 each	RC
- APS IgA Beads	- Paramagnetic beads coated with: - Native Cardiolipin (CL) plus β2GPI antigens - Native β2GPI antigen - AffiniPure Goat polyclonal anti-human IgA antigen - Bovine protein stabilizer	1 x 0.5mL	-
- Assay Buffer	- Bovine/porcine protein stabilizer - Bovine protein stabilizer - Sodium azide	1 x 17mL	-
- PE Tracer IgA	- PE IgA Conjugate, Goat anti-human IgA antibody - Bovine protein stabilizer - Sodium azide	1 x 17mL	-
- Rehydration Buffer	- Bovine protein stabilizer - Sodium azide	1 x 6.5mL	-

Intended use(s)

The Aptiva APS IgA Reagent is an immunoassay utilizing particle-based multi-analyte technology for the semi-quantitative determination of anti-cardiolipin (aCL) and anti-beta 2 glycoprotein 1 (aβ2GPI) IgA autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory and clinical findings.

The Aptiva APS IgA Reagent is intended for use with the Aptiva System.

Indications for use

Same as intended use.

Substantial equivalence

The Aptiva APS IgA Reagent have the same intended use and assay principle as the predicate devices.

Comparison to predicate device

Aptiva APS IgA Reagent - aCL IgA Assay

Aptiva APS IgA Reagent - aCL IgA Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgA Reagent, and its predicate device currently marketed as QUANTA Flash aCL IgA Reagents (K120817).		
	Subject Device	**Predicate Device**
Item	**Aptiva APS IgA Reagent (aCL IgA)**	**QUANTA Flash aCL IgA Reagents (aCL IgA)**
Trade name	Aptiva APS IgA Reagent	QUANTA Flash aCL IgA Reagents
Intended Use / Indication for Use	The Aptiva APS IgA Reagent is an immunoassay utilizing particle-based multi-analyte technology for the semi-quantitative determination of anti-cardiolipin (aCL) and anti-beta 2 glycoprotein 1 (aβ2GPI) IgA autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory and clinical findings. The Aptiva APS IgA Reagent is intended for use with the Aptiva System.	Fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgA antibodies in human citrated plasma and serum on the BIO-FLASH®, instrument, 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.
Type of Test	Semi-quantitative	Same
Instrument Platform	Aptiva System	BIO-FLASH instrument
Technology	Fluorescent immunoassay	Chemiluminescent immunoassay
Clinical Cut-off	5.00 FLU	20.0 CU
Calibrator	Three Calibrator Levels	Two Calibrator Levels
Composition	1 cartridge containing 1 vial of magnetic particle suspension coated with bovine cardiolipin and human purified ß2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgA antibody labeled with phycoerythrin, and 1 vial of sample diluent.	1 cartridge containing 1 vial of magnetic particle suspension coated with bovine cardiolipin and human purified β2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgA antibody labeled with isoluminol, and 1 vial of sample diluent.
Sample Type	Serum	Serum or Citrated Plasma
Quality Control	Two Control Levels	Same
Limit of Detection (LoD)	0.11 FLU	1.4 CU
Linearity	0.41 – 68.00 FLU	1.4 – 351.6 CU

Aptiva APS IgA Reagent - aβ2GPI IgA Assay

Aptiva APS IgA Reagent - aβ2GPI IgA Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgA Reagent, and its predicate device currently marketed as QUANTA Flash β2GPI IgA Reagents (K120817).		
Item	**Aptiva APS IgA Reagent (aβ2GPI IgA)**	**QUANTA Flash β2GPI IgA (β2GPI IgA)**
Trade name	Aptiva APS IgA Reagent	QUANTA Flash β2GPI IgA
Intended Use / Indication for Use	The Aptiva APS IgA Reagent is an immunoassay utilizing particle-based multi-analyte technology for the semi-quantitative determination of anti-cardiolipin (aCL) and anti-beta 2 glycoprotein 1 (aβ2GPI) IgA autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory and clinical findings. The Aptiva APS IgA Reagent is intended for use with the Aptiva System.	Fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-ß2 glycoprotein-1 (β2GP1) IgA antibodies in human citrated plasma and serum on the BIO-FLASH® instrument, as an aid in the diagnosis of thrombotic disorders related to primary and secondary antiphospholipid syndrome, when used in conjunction with other laboratory and clinical findings.
Type of Test	Semi-quantitative	Same
Instrument Platform	Aptiva System	BIO-FLASH instrument
Technology	Fluorescent immunoassay	Chemiluminescent immunoassay
Clinical Cut-off	5.00 FLU	20.0 CU
Calibrator	Three Calibrator Levels	Two Calibrator Levels
Composition	1 cartridge containing 1 vial of magnetic particle suspension coated with bovine cardiolipin and human purified ß2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgA antibody labeled with phycoerythrin, and 1 vial of sample diluent.	1 cartridge containing 1 vial of magnetic particle suspension coated with human purified β2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgA antibody labeled with isoluminol, and 1 vial of sample diluent.
Sample Type	Serum	Serum or Citrated Plasma
Quality Control	Two Control Levels	Same
Limit of Detection (LoD)	0.48 FLU	4.0 CU
Linearity	0.66 – 80.00 FLU	4.0 – 512.0 CU

Analytical performance characteristics

Quantitation and units of measure

For quantitation, the Aptiva APS IgA reagents utilize predefined lot specific Master Curves, one for each analyte (aCL IgA and aβ2GPI IgA) that are uploaded onto the instrument through the reagent cartridge RFID. The analyte specific Master Curves are generated at Inova for each reagent lot, where in-house Master Curve Standards with assigned FLU values are run multiple times. The resulting MFI values generated are used to create a unique 4 parameter logistic (4PL) curve for each of the two analytes. The IgA control bead will flag low concentrations of IgA antibodies in the sample as an assay verification step. This microparticle also has an in-house standard which is run each time a new reagent lot is manufactured. The MFI produced by this standard is used as the cut-off threshold for the IgA control microparticle for that reagent lot. These four parameters of the analyte curves, as well as the MFI cut-off for the IgA control microparticle are embedded in the reagent cartridge RFID.

List of Aptiva APS IgA Master Curve Standards – Assigned Value:

Material	aCL IgA - FLU	aβ2GPI IgA - FLU
APS IgA Master Curve Standard 1	0.00	0.00
APS IgA Master Curve Standard 2	0.78	1.34
APS IgA Master Curve Standard 3	3.90	7.80
APS IgA Master Curve Standard 4	19.46	37.46
APS IgA Master Curve Standard 5	72.13	109.71

IgA Control Microparticle Standard: 0.286 mg/dL human IgA

Precision

The precision of the Aptiva APS IgA reagent was evaluated on six samples for aCL IgA and aβ2GPI IgA containing various concentrations of antibodies in accordance with CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline. Samples were run in duplicates, twice a day, for 20 days.

Data were analyzed with the *Analyse-it* for Excel method evaluation software, and repeatability (within-run), between run, between day and within-laboratory precision (total precision) were calculated. Results are summarized in the two tables below.

aCL IgA Precision			Repeatability		Between Run		Between Day		Within Laboratory	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV	SD (FLU)	CV	SD (FLU)	CV	SD (FLU)	CV
Sample 1	80	1.49	0.07	5.0%	0.05	3.3%	0.08	5.6%	0.12	8.2%
Sample 2	80	3.56	0.19	5.5%	0.05	1.4%	0.23	6.5%	0.31	8.6%
Sample 3	80	5.50	0.24	4.3%	0.12	2.2%	0.32	5.8%	0.42	7.6%
Sample 4	80	11.64	0.30	2.6%	0.27	2.3%	0.51	4.4%	0.66	5.6%
Sample 5	80	24.94	0.93	3.7%	1.26	5.1%	1.15	4.6%	1.94	7.8%
Sample 6	80	45.39	1.32	2.9%	1.50	3.3%	2.16	4.8%	2.94	6.5%

aβ2GPI IgA Precision			Repeatability		Between Run		Between Day		Within Laboratory	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV	SD (FLU)	CV	SD (FLU)	CV	SD (FLU)	CV
Sample 1	80	2.05	0.14	6.7%	0.14	6.9%	0.12	5.7%	0.23	11.2%
Sample 2	80	4.82	0.30	6.2%	0.13	2.7%	0.45	9.3%	0.55	11.5%
Sample 3	80	7.43	0.35	4.7%	0.22	2.9%	0.68	9.2%	0.80	10.7%
Sample 4	80	15.58	0.49	3.2%	0.42	2.7%	0.83	5.3%	1.05	6.7%
Sample 5	80	28.44	1.08	3.8%	1.23	4.3%	1.87	6.6%	2.49	8.7%
Sample 6	80	56.85	1.49	2.6%	2.06	3.6%	3.12	5.5%	4.03	7.1%

Reproducibility Studies

Reproducibility between sites (instruments)

Seven samples for aCL IgA and aβ2GPI IgA were tested according to CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline, at three different sites. Samples were run in replicates of five, once a day, for five days, to generate 25 data points per sample, per site. Data were analyzed with the *Analyse-it* for Excel method evaluation software to calculate between site precision. Results are summarized in the following tables.

aCL IgA			Repeatability		Between Day		Between-Site		Reproducibility	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%
1	75	2.21	0.11	5.1%	0.04	1.7%	0.13	5.8%	0.18	7.9%
2	75	4.85	0.19	3.8%	0.15	3.2%	0.24	5.0%	0.34	7.1%
3	75	5.45	0.23	4.3%	0.19	3.5%	0.28	5.1%	0.41	7.6%
4	75	7.84	0.35	4.4%	0.24	3.1%	0.50	6.3%	0.65	8.3%
5	75	16.51	0.56	3.4%	0.60	3.6%	1.39	8.4%	1.61	9.8%
6	75	37.16	1.27	3.4%	0.97	2.6%	3.91	10.5%	4.23	11.4%
7	75	54.80	1.95	3.6%	0.91	1.7%	2.06	3.8%	2.98	5.4%

aβ2GPI IgA			Repeatability		Between Day		Between-Site		Reproducibility	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%
1	75	2.50	0.13	5.1%	0.08	3.2%	0.16	6.5%	0.22	8.8%
2	75	5.10	0.20	3.9%	0.17	3.4%	0.30	5.9%	0.40	7.8%
3	75	6.41	0.24	3.7%	0.22	3.4%	0.41	6.4%	0.52	8.2%
4	75	9.36	0.42	4.5%	0.17	1.8%	0.65	7.0%	0.80	8.5%
5	75	19.77	0.56	2.8%	0.65	3.3%	1.63	8.3%	1.84	9.3%
6	75	35.86	1.06	2.9%	1.06	2.9%	3.13	8.7%	3.47	9.7%
7	75	64.91	1.95	3.0%	2.98	4.6%	1.91	2.9%	4.04	6.2%

Reproducibility between lots

Five samples for aCL IgA and aβ2GPI IgA were tested according to CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline, using three different lots. Samples were run in replicates of 5, once a day, for 5 days, to generate 25 data points per sample, per lot, 75 data points total for each sample. Data were analyzed with the *Analyse-it* for Excel method evaluation software to calculate between lot precision. Results are summarized in the following tables.

aCL IgA			Repeatability		Between Day		Between-Lot		Reproducibility	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%
1	75	1.97	0.17	8.4%	0.09	4.6%	0.02	1.0%	0.19	9.6%
2	75	5.01	0.33	6.6%	0.22	4.4%	0.00	0.0%	0.40	7.9%
3	75	5.09	0.22	4.4%	0.15	2.8%	0.05	0.9%	0.27	5.3%
4	75	17.42	0.90	5.2%	0.39	2.2%	0.42	2.4%	1.07	6.1%
5	75	50.12	1.67	3.3%	0.85	1.7%	4.01	8.0%	4.43	8.8%

aβ2GPI IgA			Repeatability		Between Day		Between-Lot		Reproducibility	
Sample	Replicates (N)	Mean (FLU)	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%	SD (FLU)	CV%
1	75	2.12	0.19	9.0%	0.12	5.5%	0.11	5.1%	0.25	11.7%
2	75	5.53	0.29	5.3%	0.22	4.0%	0.34	6.1%	0.50	9.0%
3	75	5.63	0.28	4.9%	0.10	1.8%	0.25	4.5%	0.39	6.9%
4	75	26.53	1.21	4.6%	0.61	2.3%	1.15	4.3%	1.78	6.7%
5	75	60.69	1.95	3.2%	3.63	6.0%	2.99	4.9%	5.09	8.4%

Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ)

The LoB, LoD, and LoQ of the aCL IgA and aβ2GPI IgA assays in the Aptiva APS IgA Reagent were calculated separately by a study according to CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline- Second Edition.

Study protocol for LoB:
Four blank samples were run in replicates of five on two reagent lots, once per day, for 3 days, with 60 data points generated per analyte on each lot. The LoB was determined for each assay, on each reagent lot separately with the *Analyse-it* for Excel software's Reference Interval function, at the 95th percentile, using the non-parametric method for aCL IgA and aβ2GPI IgA assays (all having a p-value = <0.0001)

The aCL IgA LoB for one reagent lot was determined as 0.06 FLU, and for the second reagent lot as 0.03 FLU. The final LoB value for aCL IgA is 0.06 FLU.

The aβ2GPI IgA LoB for one reagent lot was determined as 0.38 FLU, and for the second reagent lot as 0.24 FLU. The final LoB value for aβ2GPI IgA is 0.38 FLU.

Study protocol for LoD:
Four low level samples for aCL IgA and aβ2GPI IgA assays were run in replicates of five on two reagent lots, twice per day, for 3 days, with 120 data points generated on each analyte, on each reagent lot. The LoD was determined separately for each analyte, on each reagent lot.

The aCL IgA limit of detection for one reagent lot was determined as 0.11 FLU, and for the second reagent lot as 0.09 FLU. The final LoD value for aCL IgA is 0.11 FLU.

The aβ2GPI IgA limit of detection for one reagent lot was determined as 0.48 FLU, and for the second reagent lot as 0.45 FLU. The final LoD value for aβ2GPI IgA is 0.48 FLU.

Study protocol for LoQ:
Four low level samples for aCL IgA and aβ2GPI IgA assays (prepared by mixing human serum samples with high and low levels of antibodies) were run in replicates of five on two reagent lots, twice per day, for 3 days, with 120 data points generated on each analyte, on each reagent lot. The LoQ was determined separately for each analyte, on each reagent lot. The LoQ was determined in each case by calculating the total imprecision of each.

The aCL IgA LoQ for one reagent lot was determined as 0.23 FLU, and for the second reagent lot as 0.20 FLU. The determined LoQ value is 0.23 FLU. The claimed LoQ is 0.41 FLU which is the lower limit of the analytical measuring range of the aCL IgA assay.

The aβ2GPI IgA LoQ for both reagent lots was determined as 0.49 FLU. The claimed LoQ is 0.66 FLU which is the lower limit of the analytical measuring range of the aβ2GPI IgA assay.

Analytical Measuring Range (AMR)

Within the Aptiva APG IgA Reagent:

aCL IgA:	0.41 – 68.00 FLU
aβ2GPI IgA:	0.66 – 80.00 FLU

High concentration hook effect

To assess hook effect, three samples for aCL IgM and aβ2GPI IgM assays were tested at increasing 2-fold serial dilutions on the Aptiva APS IgA Reagent. All FLU values above the analytical measuring are theoretical and were mathematically calculated using the 4 parameters of their respective calibration curves. All samples showed increase in FLU values as the samples became more concentrated, thereby confirming that high positive specimens above the AMR do not show hook effect up to 98.19 FLU for aCL IgA and 133.48 FLU for the aβ2GPI IgA (theoretical values calculated) in the Aptiva APS IgA Reagents.

Linearity

The Linearity of the AMR was calculated separately for aCL IgA and aβ2GPI IgA assays as part of the Aptiva APS IgA Reagent.

The linearity of the AMR of aCL IgA and aβ2GPI IgA was evaluated by a study according to CLSI EP06, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline – Second Edition. Four human serum samples for aCL IgA and three human serum samples for aβ2GPI IgA with various antibody concentrations were serially diluted to obtain values that cover the entire AMR. The dilutions were assayed in duplicates. Results were analyzed according to the guideline performing regression analysis and identifying the best fitting polynomial.

aCL IgA:

Sample	Test Range (FLU)	Slope (95% CI)	R^2	Range of Linearity Deviations (%)	Range of Linearity Deviations (FLU)
1	301.63 - 30.16	1.07 (1.03 - 1.12)	0.99	-6.8% to 10.4%	N/A
2	55.11 - 5.51	1.00 (0.97 - 1.03)	1.00	-7.9% to 5.0%	N/A
3	27.20 - 2.72	1.02 (1.00 - 1.03)	1.00	-1.8% to 6.6%	0.48 FLU
4	4.05 - 0.41	1.00 (0.95 - 1.05)	1.00	-14.1% to 6.4%	-0.19 to -0.15 FLU
Combined	301.63 – 0.41	0.93 (0.91 – 0.95)	1.00	-14.1% to 10.4%	-0.19 to 0.48 FLU

aβ2GPI IgA:

Sample	Test Range (FLU)	Slope (95% CI)	R^2	Range of Linearity Deviations (%)	Range of Linearity Deviations (FLU)
1	12.57 - 1.26	0.94 (0.90 - 0.98)	0.99	-11.7% to 6.7%	-0.48 FLU
2	81.66 - 8.17	1.00 (0.97 - 1.03)	1.00	-13.9% to 5.1%	N/A
3	5.71 - 0.57	0.99 (0.94 - 1.04)	0.99	-4.2% to 6.1% and	-0.44 to -0.18 FLU
Combined	81.66 – 0.57	0.99 (0.97 – 1.00)	1.00	-13.9% to 6.7%	-0.48 to -0.18 FLU

These data demonstrate the linearity of the analytical measuring range (0.41 – 68.00 FLU) of the aCL IgA analyte and the analytical measuring range (0.66 – 80.00 FLU) of the aβ2GPI IgA analyte, both as part of the Aptiva APS IgA Reagent.

Interference

The interference study was performed according to CLSI EP07, Interference Testing in Clinical Chemistry; Approved Guideline - Third Edition. Three human serum (one positive, one around the cutoff and one negative sample) were tested. Endogenous interfering substances (bilirubin, hemoglobin, triglycerides, cholesterol, rheumatoid factor IgM and human IgG) and exogenous substances (ibuprofen, warfarin, prednisone, acetaminophen, aspirin, hydroxychloroquine, omeprazole, simvastatin and heparin) were spiked into each serum and the resulting samples were assessed in five replicates with the aCL IgA and aβ2GPI Ig assays as part of the Aptiva APS IgA Reagent. Recovery of the unit values was calculated compared to control samples.

No interference was detected for aCL IgA and aβ2GPI IgA with endogenous substance for bilirubin at 100.0 mg/dL, triglycerides at 1000.0 mg/dL, cholesterol at 332.5 mg/dL, RF IgM at 196.5 IU/mL, human IgG at 2000 mg/dL, and hemoglobin at 10.0 g/L.

No interference was detected for aCL IgA and aβ2GPI IgA with exogenous substances at 21.9 mg/dL ibuprofen, 7.5 mg/dL warfarin, 0.0099 mg/dL prednisone, 15.6 mg/dL acetaminophen, 3.0 mg/dL of aspirin, 0.465 mg/dL of hydroxychloroquine, 0.84 mg/dL of omeprazole, 0.168 mg/dL of simvastatin, and 330.0 units/dL of heparin.

Aptiva APS IgA Reagent - aCL IgA		**Percent Recovery or FLU Difference**		
Endogenous Interfering substance	Final Conc.	Negative	Borderline	Positive
Bilirubin, Conjugated	100.0 mg/dL	100.5%	86.8%	99.1%
Triglyceride	1000.0 mg/dL	97.3%	100.6%	100.9%
Cholesterol	332.5 mg/dL	104.5%	104.5%	98.9%
RF IgM	196.5 IU/mL	101.3%	107.7%	98.8%
Human IgG	2000.0 mg/dL	95.7%	102.0%	101.0%
Hemoglobin	10.0 g/L	96.1%	98.7%	108.8%
Exogenous Interfering substance	Final Conc.	Negative	Borderline	Positive
Ibuprofen	21.9 mg/dL	107.7%	99.5%	104.4%
Warfarin	7.5 mg/dL	99.3%	99.7%	102.0%
Prednisone	0.0099 mg/dL	97.8%	100.8%	101.5%
Acetaminophen	15.6 mg/dL	97.1%	96.7%	101.0%
Aspirin	3.0 mg/dL	101.0%	106.0%	109.3%
Hydroxychloroquine	0.465 mg/dL	98.1%	107.6%	111.5%
Omeprazole	0.84 mg/dL	103.9%	94.9%	99.3%
Simvastatin	0.168 mg/dL	107.8%	97.5%	109.2%
Heparin	330.0 units/dL	109.8%	111.8%	106.1%

Aptiva APS IgA Reagent - aβ2GPI IgA		Percent Recovery or FLU Difference		
Endogenous Interfering substance	Final Conc.	Negative	Borderline	Positive
Bilirubin	100.0 mg/dL	96.9%	89.2%	97.8%
Triglyceride	1000.0 mg/dL	101.7%	96.8%	101.4%
Cholesterol	332.5 mg/dL	0.57 FLU	103.7%	99.2%
RF IgM	196.5 IU/mL	114.9%	100.3%	100.1%
Human IgG	2000.0 mg/dL	93.7%	103.1%	102.1%
Hemoglobin	10.0 g/L	95.0%	97.7%	105.7%
Exogenous Interfering substance	Final Conc.	Negative	Borderline	Positive
Ibuprofen	21.9 mg/dL	101.3%	97.4%	103.6%
Warfarin	7.5 mg/dL	106.2%	97.6%	102.4%
Prednisone	0.0099 mg/dL	106.4%	98.2%	101.1%
Acetaminophen	15.6 mg/dL	105.3%	97.2%	101.9%
Aspirin	3.0 mg/dL	103.5%	105.2%	106.8%
Hydroxychloroquine	0.465 mg/dL	103.5%	99.7%	108.7%
Omeprazole	0.84 mg/dL	110.5%	102.3%	99.7%
Simvastatin	0.168 mg/dL	109.3%	99.3%	108.7%
Heparin	330.0 units/dL	108.6%	109.3%	105.7%

Sample Stability and Handling

For the aCL IgA and aβ2GPI IgA analytes, three serum samples were tested. The samples used for this study were achieved by combining high and low antibody levels to yield their desired reactivity. All samples were tested in duplicates for up to 22 days while stored at 2-8°C, up to 50 hours while stored at room temperature (20-26°C), and after repeated freeze/thaw cycles up to five cycles. Results were compared to those obtained on control samples (time zero / zero cycles).

All samples fulfilled the acceptance criteria at each time point for each condition. Based on these results, we recommend that samples may be stored up to 48 hours at room temperature, up to 14 days at 2-8°C and can be subjected to up to four freeze/thaw cycles.

Reagent Stability

Shelf life

To establish the initial claim for shelf life for the Aptiva APS IgA Reagent accelerated stability studies were performed on three lots of reagents for 5 weeks at 37°C ± 3°C, where one week is equal to six months at 5 ± 3°C.

Each week a new sealed reagent was placed in the incubator, and all reagents were tested at the end of the experiment together with the one that was stored at 5 ± 3°C. The recovery of the measured values was calculated for each time point (compared to those obtained with 5 ± 3°C stored reagent). All calculations were performed by comparing results of sealed components stored at 5 ± 3°C (control) to those stored at 37 ± 3°C (test) for 1, 2, 3, 4, and 5 weeks, where one

week is equal to six months at 5 ± 3°C. Linear regression analysis was performed between recovery values and the number of days.

All reagents tested fulfilled the acceptance criteria above, therefore, 11-month expiration dating was assigned to the Aptiva APS IgA Reagent.

Real time stability

Real-time stability testing has been scheduled on the Aptiva APS IgA Reagent, to verify the assigned expiration dating based on accelerated stability studies. Real-time test samples consisted of the following: low negative, mid negative, high negative (near the assay cutoff), low positive (near assay cutoff), mid positive, and high positive.

In-use (onboard) stability

Reagent Cartridge

To establish the in-use stability of the Aptiva APS IgA Reagent, one lot of reagent was tested using seven samples (with different reactivity levels) and two controls periodically for 29 days. On Day 14, the reagent was recalibrated, and a specific Working Curve was generated. Percent recoveries were calculated compared to the Day 0 average values, and linear regression analysis was performed by plotting percent recovery against the number of days.

The in-use (onboard) stability of the Aptiva APS IgA Reagent was set at 28 days, with a 14-day recalibration.

Cut-off, reference range

The following cut-off is used for the aCL IgA and aβ2GPI IgA assays in the Aptiva APS IgA Reagent:

Negative	<5.00 FLU
Positive	≥5.00 FLU

The reference population for establishing the cutoff values for the aCL IgA and aβ2GPI IgA analytes in the Aptiva APS IgA Reagent consisted of testing 232 disease control samples.

The cut-off values were established in accordance with CLSI EP28-A3c: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition. The *Analyse-it* for Excel software was used to make the calculations. The distribution of the results was non-normal (Shapiro-Wilk $p<0.0001$), therefore the non-parametric percentile method was used.

The cut-off was established based on greater than the 95th percentile of the results obtained on the disease control population.

For the Aptiva APS IgA Reagent (including the aCL IgA and aβ2GPI IgA analytes) based on the distribution of result values of disease controls the cutoff was established at 95 MFI for aCL IgA and 85 MFI for aβ2GPI IgA and was assigned a value of 5.00 FLU. With this cutoff, we ensure

that the cutoff value is greater than the 95th percentile on reference healthy population (75 MFI and 79 MFI for aCL IgA and for aβ2GPI IgA, respectively).

Clinical performance characteristics

Clinical sensitivity, specificity

A cohort of characterized samples, none of which were used for establishing the reference range, was used to validate the clinical performance of the Aptiva APS IgA Reagent.

For Aptiva APS IgA Reagent, a total of 615 characterized samples were included in this Validation Set, including 153 samples from APS patients (70 primary APS and 83 secondary APS) and 462 control samples from patients with various types of autoimmune and infectious diseases. All samples were run on the Aptiva APS IgA Reagent. The distribution of the cohort and the aCL IgA and aβ2GPI IgA positivity rate is in the following table:

Patient Group	N=615	aCL IgA No. Positive	aCL IgA % Positive	aβ2GPI No. Positive	aβ2GPI % Positive
APS combined	**153**	**48**	**31.4%**	**49**	**32.0%**
pAPS	70	14	20.0%	17	24.3%
sAPS	83	34	41.0%	32	38.6%
Controls	**462**	**10**	**2.2%**	**7**	**1.5%**
Viral Infectious Disease	53	2	3.8%	0	0.0%
Bacterial Infectious Disease	45	2	4.4%	0	0.0%
Myositis	24	0	0.0%	0	0.0%
Preeclampsia or Placental Insufficiency (PREPI)	36	0	0.0%	0	0.0%
Systemic Lupus Erythematosus (SLE) (without APS)	34	1	2.9%	1	2.9%
Inflammatory Bowel Disease (IBD)	19	0	0.0%	0	0.0%
Rheumatoid Arthritis (RA)	20	0	0.0%	0	0.0%
Fetal loss (without APS)	13	0	0.0%	0	0.0%
Thrombosis (without APS)	1	0	0.0%	0	0.0%
ANCA-Associated Vasculitis	18	0	0.0%	0	0.0%
Autoimmune Thyroiditis	49	1	2.0%	2	4.1%
Celiac Disease (CeD)	44	1	2.3%	0	0.0%
COVID-19 Related Thrombosis	22	0	0.0%	0	0.0%
Hematologic Malignancies	20	1	5.0%	1	5.0%
Idiopathic thrombocytopenic purpura (ITP)	14	1	7.1%	1	7.1%
Solid Tumor Malignancies	20	0	0.0%	1	5.0%
Deep Vein Thrombosis	18	1	5.6%	1	5.6%
Myocardial Infarction (MI)	12	0	0.0%	0	0.0%

Clinical sensitivity and specificity for the Aptiva APS IgA Reagent - aCL IgA were analyzed in the following table:

Clinical Analysis (N=615)			Diagnosis		
			APS	Controls	Totals
Aptiva APS IgA (aCL IgA)	Positive	≥5.0	48	10	58
	Negative	<5.0	105	452	557
	Total		153	462	615

Sensitivity	31.4%	(24.6 - 39.1%)
Specificity	97.8%	(96.1 - 98.8%)

Clinical sensitivity and specificity for the Aptiva APS IgA Reagent aβ2GPI IgA were analyzed in the following table:

Clinical Analysis (N=615)			**Diagnosis**		
			APS	Controls	Totals
Aptiva APS IgA (aβ2GPI IgA)	Positive	≥5.0	49	7	56
	Negative	<5.0	104	455	559
	Total		153	462	615

Sensitivity	32.0%	(25.2 - 39.8%)
Specificity	98.5%	(96.9 - 99.3%)

Expected values

The expected value in the normal population is “negative”. A panel of 126 apparently healthy blood donors (53 females/73 males, ages 18 to 70 years, with an average age of 38 years and median age of 35 were tested on the Aptiva APS IgA Reagent.

For Aptiva APS IgA, the aCL IgA with a cut-off of 5.00 FLU, two samples were positive, with a mean concentration of 0.73 FLU, and values ranging from 0.41 to 9.13 FLU (2.0% of the samples in the positive range). For aβ2GPI IgA, with a cut-off of 5.00 FLU, no samples were positive, with a mean concentration of 0.67 FLU, and values ranging from 0.66 to 1.52 FLU.

Comparison with predicate device

For aCL IgA, samples for method comparison analysis included 332 clinically defined samples from the clinical validation study and eight additional samples within the analytical measuring range (AMR) in order to meet the minimum requirement of 10% of the samples around the cutoff. For aβ2GPI IgA, samples for method comparison analysis included 362 clinically defined samples from the clinical validation study and twelve additional samples within the AMR to meet the

minimum requirement of 100 samples within the AMR and 10% of the samples around the cutoff. These samples were tested on both the Aptiva APS IgA Reagent and on their predicate QUANTA Flash aCL IgA and QUANTA Flash β2GP1 IgA Reagents, respectively.

Method comparison of the Aptiva APS IgA - aCL IgA with the predicate device – All Samples

Method Comparison (N=340)		QUANTA Flash aCL IgA		
		Positive	Negative	Total
Aptiva APS IgA (aCL IgA)	Positive ≥ 5.00	37	6	43
	Negative < 5.00	4	293	297
	Total	41	299	340

PPA	90.2%	(77.5 - 96.1%)
NPA	98.0%	(95.7 - 99.1%)
TPA	97.1%	(94.7 - 98.4%)

PPA: Positive Percent Agreement; NPA: Negative Percent Agreement; TPA: Total Percent

Method comparison of the Aptiva APS IgA - aCL IgA with the predicate device – Samples within AMR

Method Comparison (N=246)		QUANTA Flash aCL IgA		
		Positive	Negative	Total
Aptiva APS IgA (aCL IgA)	Positive ≥ 5.00	31	6	37
	Negative < 5.00	4	205	209
	Total	35	211	246

PPA	88.6%	(74.0 - 95.5%)
NPA	97.2%	(93.9 - 98.7%)
TPA	95.9%	(92.7 - 97.8%)

PPA: Positive Percent Agreement; NPA: Negative Percent Agreement; TPA: Total Percent

Method comparison of the Aptiva APS IgA - aβ2GPI IgA with the predicate device – All Samples

Method Comparison (N=374)		QUANTA Flash β2GPI IgA		
		Positive	Negative	Total
Aptiva APS IgA (aβ2GPI IgA)	Positive ≥ 5.00	44	9	53
	Negative < 5.00	3	318	321
	Total	47	327	374

PPA	93.6%	(82.8 - 97.8%)
NPA	97.2%	(94.9 - 98.5%)
TPA	96.8%	(94.5 - 98.2%)

PPA: Positive Percent Agreement; NPA: Negative Percent Agreement; TPA: Total Percent

Method comparison of the Aptiva APS IgA - aβ2GPI IgA with the predicate device – Sample within AMR

Method Comparison (N=100)		QUANTA Flash β2GPI IgA		
		Positive	Negative	Total
Aptiva APS IgA (aβ2GPI IgA)	Positive ≥ 5.00	37	9	46
	Negative < 5.00	3	51	54
	Total	40	60	100

PPA	92.5%	(80.1 - 97.4%)
NPA	85.0%	(73.9 - 91.9%)
TPA	88.0%	(80.2 - 93.0%)

PPA: Positive Percent Agreement; NPA: Negative Percent Agreement; TPA: Total Percent