December 17, 2024

Inova Diagnostics, Inc.
Constance Bridges
VP, Quality & Regulatory Affairs
9900 Old Grove Road
San Diego, California 92131

Re: K223093
Trade/Device Name: Aptiva APS IgG Reagent
Aptiva APS IgM Reagent
Regulation Number: 21 CFR 866.5660
Regulation Name: Multiple Autoantibodies Immunological Test System
Regulatory Class: Class II
Product Code: MID, MSV
Dated: December 14, 2023
Received: December 15, 2023

Dear Constance Bridges:

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)*
K223093

Device Name
Aptiva APS IgG Reagent
Aptiva APS IgM Reagent

Indications for Use *(Describe)*

The Aptiva APS IgG 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) IgG autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory findings.

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

The Aptiva APS IgM 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) IgM autoantibodies in human serum as an aid in the diagnosis of primary and secondary antiphospholipid syndrome (APS), when used in conjunction with other laboratory findings.

The Aptiva APS IgM 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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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

Purpose of submission: New device

Device in the submission: Aptiva APS IgG Reagent
Aptiva APS IgM Reagent

Scientific contact: Andrea Seaman, Associate Director, Research and Development
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Quality Systems contact: Constance Bridges, VP, Quality and Regulatory
Inova Diagnostics, Inc
9900 Old Grove Road, San Diego, CA, 92131
Phone: 858-586-9900 x77212
Fax: 858-863-0025
Email: cbridges@werfen.com

Device name (kit):

Proprietary name:	Aptiva APS IgG Reagent Aptiva APS IgM 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

HemosIL™ AcuStar Anti-Cardiolipin IgG, 510(k) number: K092181
QUANTA Lite™ Beta 2GP1 IgG ELISA, 510(k) number: K970551
HemosIL™ AcuStar Anti-Cardiolipin IgM, 510(k) number: K092181
HemosIL™ AcuStar Anti-β_2 Glycoprotein-I IgM, 510(k) number: K091556

Device description

The Aptiva APS IgG and Aptiva APS IgM reagent utilize particle based multi-analyte technology (PMAT) in a cartridge format. Each analyte (anti-cardiolipin [aCL] and anti-B2-Glycoprotein I [aB2GPI]) in the Aptiva APS IgG and Aptiva APS IgM reagent is a solid phase immunoassay utilizing fluorescent microparticles. This technology allows each of the two analytes, along with a human IgG or human IgM capture antibody (IgG or IgM 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 IgG or IgM antibodies, is present in the reagent as a control to flag low concentrations of IgG or IgM 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 IgG or IgM, which is proportional to the concentration of IgG or IgM 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 IgG Reagent and the Aptiva APS IgM 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 IgG and Aptiva APS IgM Calibrators and Aptiva APS IgG and Aptiva APS IgM Controls are sold separately.

The Aptiva APS IgG Reagent kit contains the following materials:

Contents	Active Ingredient	Quantity	Symbol
1. Aptiva APS IgG Reagent Cartridge	-	1 each	RC
- APS IgG Beads	- Paramagnetic beads coated with: - Native Cardiolipin (CL) plus β2GPI antigens (<0.01%) - Native β2GPI antigen (<0.5%) - AffiniPure Goat polyclonal anti-human IgG antigen (<0.01%) - Bovine protein stabilizer (<2.4%)	1 x 0.5mL	-
- Assay Buffer	- Bovine/porcine protein stabilizer (<0.5%) - Bovine protein stabilizer (<0.3%) - Sodium azide (<0.1%)	1 x 17mL	-
- PE Tracer IgG	- PE IgG Conjugate, Goat anti-human IgG antibody (<0.30%) - Bovine protein stabilizer (<1.2%) - Sodium azide (<0.1%)	1 x 17mL	-
- Rehydration Buffer	- Bovine protein stabilizer (<0.03%) - Sodium azide (<0.1%)	1 x 6.5mL	-

The Aptiva APS IgM Reagent kit contains the following materials:

Contents	Active Ingredient	Quantity	Symbol
1. Aptiva APS IgM Reagent Cartridge	-	1 each	RC
- APS IgM Beads	- Paramagnetic beads coated with: - Native Cardiolipin (CL) plus β2GPI antigens (<0.01%) - Native β2GPI antigen (<0.04%) - AffiniPure Goat polyclonal anti-human IgM antigen (<0.01%) - Bovine protein stabilizer (<2.4%)	1 x 0.5mL	-
- Assay Buffer	- Bovine/porcine protein stabilizer (<0.42%) - Bovine protein stabilizer (<0.27%) - Sodium azide (<0.1%)	1x 17mL	-
- PE Tracer IgM	- PE IgG Conjugate, Goat anti-human IgM antibody (<0.15%) - Bovine protein stabilizer (<1.2%) - Sodium azide (<0.1%)	1 x 17mL	-
- Rehydration Buffer	- Bovine protein stabilizer (< 0.02%) - Sodium azide (<0.1%)	1 x 6.5mL	

Intended use(s)

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

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

Indications for use

Same as intended use.

Substantial equivalence

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

Comparison to predicate device

Aptiva APS IgG Reagent - aCL IgG Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgG Reagent, and its predicate device currently marketed as QUANTA Flash aCL IgG Reagent. The QUANTA Flash aCL IgG Reagent is equivalent to the HemosIL AcuStar Anti-Cardiolipin IgG assay (K092181).		
	Subject Device	**Predicate Device**
Item	**Aptiva APS IgG Reagent (aCL IgG)**	**QUANTA Flash aCL IgG Reagents (aCL IgG)**
Trade name	Aptiva APS IgG Reagent	QUANTA Flash aCL IgG Reagents
Intended Use / Indication for Use	The Aptiva APS IgG 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) IgG 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 IgG Reagent is intended for use with the Aptiva Multi-Analyte System.	Fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgG 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* (20 U/mL†)
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 IgG 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 ß2GPI, 1 vial of assay buffer, 1 vial of tracer consisting of an anti-human IgG antibody labeled with isoluminol, and 1 vial of sample diluent.
Sample Type	Serum	Serum or Citrated Plasma
Quality Control	Two Control Levels	Same
Detection Limit	0.07 FLU	2.6 CU* (20 U/mL†)
Linearity	0.29 FLU – 328.94 FLU	2.6 – 2024 U/mL

* Applicable to QUANTA Flash aCL IgG Reagent

† Applicable to HemosIL AcuStar Anti-Cardiolipin IgG

Aptiva APS IgG Reagent - β2GPI IgG Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgG Reagent, and its predicate device, the currently marketed QUANTA Lite Beta 2GP1 IgG ELISA (K970551).		
Item	**Aptiva APS IgG Reagent (β2GPI IgG)**	**QUANTA Lite Beta 2GP1 IgG ELISA (aCL IgG)**
Trade name	Aptiva APS IgG Reagent	QUANTA Lite Beta 2GP1 IgG ELISA
Intended Use / Indication for Use	The Aptiva APS IgG 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) IgG 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 IgG Reagent is intended for use with the Aptiva Multi-Analyte System.	QUANTA Lite Beta 2GP1 IgG is an enzyme-linked immunosorbent assay (ELISA) for the semi-quantitative detection of β2 GPI IgG antibodies in human serum. The presence of β2 GPI IgG antibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of certain autoimmune disease thrombotic disorders, such as those secondary to systemic lupus erythematosus (SLE) or other lupus-like thrombotic diseases.
Type of Test	Semi-quantitative	Same
Instrument Platform	Aptiva Multi-Analyte System	N/A – manually run assay
Technology	Fluorescent immunoassay	Enzyme-linked immunosorbent assay
Clinical Cut-off	5.00 FLU	20.0 SGU
Calibrator	Three Calibrator Levels	Five 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 IgG antibody labeled with phycoerythrin, and 1 vial of sample diluent.	Kit contains 1 β2 GPI ELISA Plate (12-1 x 8 wells), 1 vial prediluted ELISA Negative Control, 1 vial prediluted β2 GPI IgG ELISA Control, 5 vials prediluted β2 GPI IgG ELISA Calibrators, 1 vial HRP Sample Diluent, 1 vial HRP Wash Concentrate (40x), 1 vial HRP IgG Conjugate, (goat), anti-human IgG, 1 vial 10mL TMB Chromogen, and 1 vial HRP Stop Solution
Sample Type	Serum	Same
Quality Control	Two Control Levels	Two Controls – one positive and one negative
Linearity	0.21 – 256.70 FLU	9.4 – 150.0 SGU

Aptiva APS IgM Reagent - aCL IgM Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgM Reagent, and its predicate device currently marketed QUANTA Flash aCL IgM Reagent. The QUANTA Flash aCL IgM Reagent is equivalent to the HemosIL AcuStar Anti-Cardiolipin IgM assay (K092181).		
Item	**Aptiva APS IgM Reagent (aCL IgM)**	**QUANTA Flash aCL IgG Reagents (aCL IgM)**
Trade name	Aptiva APS IgM Reagent	QUANTA Flash aCL IgM Reagents
Intended Use / Indication for Use	The Aptiva APS IgM 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) IgM 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 IgM Reagent is intended for use with the Aptiva Multi-Analyte System.	Fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-cardiolipin (aCL) IgG 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 Multi-Analyte System	BIO-FLASH instrument
Technology	Fluorescent immunoassay	Chemiluminescent immunoassay
Clinical Cut-off	5.00 FLU	20.0 CU* (20U/mL†)
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 IgM 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 ß2GPI, 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.
Sample Type	Serum	Serum or Citrated Plasma
Quality Control	Two Control Levels	Two Control Levels l
Detection Limit	0.04 FLU	1.0 CU* (1 U/mL†)
Linearity	0.10 FLU – 114.68 FLU	1.0 – 774 CU* (1.0 – 774 U/mL†)

* Applicable to QUANTA Flash aCL IgM Reagent

† Applicable to HemosIL AcuStar Anti-Cardiolipin IgM

Aptiva APS IgM Reagent - β2GPI IgM Comparison to Predicate Device		
This table provides a comparative description of the similarities and differences between the subject device, Aptiva APS IgM Reagent, and its predicate device, the currently marketed QUANTA Flash aCL IgM Reagent. The QUANTA Flash β2GPI IgM Reagent is equivalent to the HemosIL AcuStar Anti-β2 Glycoprotein-I IgM assay (K091556).		
Item	**Aptiva APS IgM Reagent (β2GPI IgM)**	**QUANTA Flash β2GPI IgM Reagents (β2GPI IgM)**
Trade name	Aptiva APS IgM Reagent	QUANTA Flash β2GPI IgM Reagents
Intended Use / Indication for Use	The Aptiva APS IgM 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) IgM 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 IgM Reagent is intended for use with the Aptiva Multi-Analyte System.	Fully automated chemiluminescent immunoassay for the semi-quantitative measurement of anti-β2 glycoprotein-1 (β2GP1) IgM 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 Multi-Analyte System	BIO-FLASH instrument
Technology	Fluorescent immunoassay	Chemiluminescent immunoassay
Clinical Cut-off	5.00 FLU	20.0 CU* (20 U/mL†)
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 IgM 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 ß2GPI, 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.
Sample Type	Serum	Serum or Citrated Plasma
Quality Control	Two Control Levels	Two levels at or near cut-off and at abnormal level
Detection Limit	0.04 FLU	1.1 CU* (1.1 U/mL†)
Linearity	0.10 FLU – 95.86 FLU	1.0 – 841 CU* (1.0 – 841 U/mL†)

* Applicable to QUANTA Flash β2GPI IgM Reagent

† Applicable to HemosIL AcuStar Anti-β2 Glycoprotein-I IgM

Analytical performance characteristics

Quantitation and units of measure

For quantitation, the Aptiva APS IgG and Aptiva APS IgM reagents utilize predefined lot specific Master Curves, one for each analyte (aCL IgG, aβ2GP1 IgG, aCL IgM and aβ2GPI IgM) 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 IgG and IgM control bead will flag low concentrations of IgG or IgM 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 IgG or IgM control microparticle for that reagent lot. These four parameters of the analyte curves, as well as the MFI cut-off for the IgG or IgM control microparticle are embedded in the reagent cartridge RFID.

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

Material	aCL IgG - FLU	aβ2GPI IgG - FLU
APS IgG Master Curve Standard 1	0.00	0.00
APS IgG Master Curve Standard 2	1.28	1.00
APS IgG Master Curve Standard 3	5.14	4.01
APS IgG Master Curve Standard 4	20.56	16.04
APS IgG Master Curve Standard 5	82.24	64.17
APS IgG Master Curve Standard 6	328.94	256.70

IgG Control Microparticle Standard: 1 mg/dL human IgG

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

Material	aCL IgM - FLU	aβ2GPI IgM- FLU
APS IgM Master Curve Standard 1	0.00	0.00
APS IgM Master Curve Standard 2	1.42	1.18
APS IgM Master Curve Standard 3	4.25	3.55
APS IgM Master Curve Standard 4	12.74	10.65
APS IgM Master Curve Standard 5	38.23	31.95
APS IgM Master Curve Standard 6	114.68	95.86

IgM Control Microparticle Standard: 1.5 mg/dL human IgM

Precision

The precision of the Aptiva APS IgG and Aptiva APS IgM reagents was evaluated on seven samples for aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM, 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 IgG 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
aCL Sample 1	80	2.33	0.13	5.5%	0.08	3.3%	0.10	4.3%	0.18	7.8%
aCL Sample 2	80	5.64	0.29	5.1%	0.10	1.8%	0.28	5.0%	0.42	7.4%
aCL Sample 3	80	8.77	0.37	4.2%	0.32	3.7%	0.00	0.0%	0.49	5.6%
aCL Sample 4	80	26.15	1.41	5.4%	0.00	0.0%	1.42	5.4%	2.00	7.6%
aCL Sample 5	80	66.29	2.53	3.8%	2.22	3.4%	2.71	4.1%	4.32	6.5%
aCL Sample 6	80	201.45	7.94	3.9%	5.58	2.8%	10.65	5.3%	14.40	7.2%
aCL Sample 7	80	265.15	11.06	4.2%	10.94	4.1%	19.96	7.5%	25.30	9.5%

aβ2GPI IgG 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
aβ2GPI Sample 1	80	2.04	0.15	7.3%	0.04	1.9%	0.18	9.0%	0.24	11.7%
aβ2GPI Sample 2	80	5.12	0.29	5.7%	0.22	4.4%	0.00	0.0%	0.37	7.1%
aβ2GPI Sample 3	80	9.39	0.50	5.3%	0.29	3.1%	0.89	9.5%	1.06	11.3%
aβ2GPI Sample 4	80	24.55	1.22	5.0%	0.22	0.9%	1.69	6.9%	2.10	8.5%
aβ2GPI Sample 5	80	53.51	2.11	3.9%	2.08	3.9%	2.22	4.1%	3.70	6.9%
aβ2GPI Sample 6	80	170.02	6.40	3.8%	5.05	3.0%	7.83	4.6%	11.30	6.6%
aβ2GPI Sample 7	80	212.10	8.19	3.9%	6.60	3.1%	14.44	6.8%	17.86	8.4%

aCL IgM 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
aCL Sample 1	80	2.93	0.12	4.1%	0.06	2.1%	0.25	8.5%	0.28	9.7%
aCL Sample 2	80	5.54	0.15	2.8%	0.10	1.9%	0.20	3.6%	0.27	4.9%
aCL Sample 3	80	10.67	0.34	3.2%	0.14	1.3%	0.50	4.7%	0.62	5.8%
aCL Sample 4	80	21.94	0.59	2.7%	0.55	2.5%	0.51	2.3%	0.95	4.3%
aCL Sample 5	80	56.16	1.30	2.3%	0.47	0.8%	3.07	5.5%	3.36	6.0%
aCL Sample 6	80	73.51	2.25	3.1%	1.23	1.7%	3.06	4.2%	3.99	5.4%
aCL Sample 7	80	116.09	2.62	2.3%	2.55	2.2%	5.90	5.1%	6.94	6.0%

aβ2GPI IgM 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
aβ2GPI Sample 1	80	2.47	0.10	3.9%	0.07	2.9%	0.22	9.0%	0.25	10.2%
aβ2GPI Sample 2	80	5.39	0.13	2.5%	0.27	5.0%	0.22	4.1%	0.38	7.0%
aβ2GPI Sample 3	80	8.75	0.28	3.2%	0.19	2.1%	0.38	4.4%	0.51	5.8%
aβ2GPI Sample 4	80	27.26	1.23	4.5%	0.51	1.9%	1.37	5.0%	1.91	7.0%
aβ2GPI Sample 5	80	46.00	1.22	2.7%	0.74	1.6%	2.29	5.0%	2.70	5.9%
aβ2GPI Sample 6	80	63.00	2.10	3.3%	0.63	1.0%	2.70	4.3%	3.48	5.5%
aβ2GPI Sample 7	80	93.18	2.97	3.2%	2.03	2.2%	4.59	4.9%	5.83	6.3%

Reproducibility Studies

Reproducibility between sites (instruments)

Seven samples for aCL IgG and aβ2GPI IgG and six samples for aCL IgM and aβ2GPI IgM 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 tables below.

aCL IgG			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	1.97	0.10	5.2%	0.04	2.3%	0.12	6.0%	0.16	8.3%
2	75	5.60	0.33	5.9%	0.20	3.6%	0.13	2.3%	0.41	7.2%
3	75	25.24	1.35	5.3%	1.06	4.2%	0.49	1.9%	1.78	7.1%
4	75	53.83	2.46	4.6%	1.48	2.7%	1.40	2.6%	3.19	5.9%
5	75	123.94	6.00	4.8%	2.43	1.0%	0.00	0.0%	6.48	5.2%
6	75	164.49	9.10	5.5%	5.26	3.2%	2.78	1.7%	10.87	6.6%
7	75	279.39	14.03	5.0%	5.79	2.1%	20.98	7.5%	25.89	9.3%

aβ2GPI IgG			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	1.99	0.11	5.7%	0.08	4.0%	0.14	7.1%	0.20	10.0%
2	75	5.26	0.24	4.6%	0.20	3.8%	0.19	3.6%	0.36	6.9%
3	75	23.58	1.08	4.6%	1.18	5.0%	0.96	4.1%	1.87	7.9%
4	75	52.83	2.49	4.7%	1.76	3.3%	1.47	2.8%	3.38	6.4%
5	75	138.12	8.47	6.1%	4.03	2.9%	7.36	5.3%	11.92	8.6%
6	75	161.78	6.16	3.8%	4.09	2.5%	10.78	6.7%	13.07	8.1%
7	75	217.27	9.54	4.4%	4.86	2.2%	12.35	5.7%	16.35	7.5%

aCL IgM			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	2.16	0.10	4.6%	0.09	4.3%	0.05	2.2%	0.14	6.7%
2	75	4.56	0.16	3.4%	0.19	4.1%	0.04	0.8%	0.24	5.4%
3	75	6.68	0.28	4.1%	0.19	2.8%	0.33	5.0%	0.47	7.1%
4	75	40.83	1.47	3.6%	1.33	3.3%	3.56	8.7%	4.07	10.0%
5	75	57.09	2.30	4.0%	1.61	2.8%	4.83	8.5%	5.59	9.8%
6	75	92.71	4.27	4.6%	2.36	2.5%	8.24	8.9%	9.58	10.3%

aβ2GPI IgM			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	1.56	0.06	3.7%	0.06	3.9%	0.04	2.3%	0.09	5.9%
2	75	4.63	0.17	3.7%	0.14	3.0%	0.18	3.9%	0.28	6.2%
3	75	6.11	0.24	3.9%	0.20	3.3%	0.36	5.9%	0.47	7.8%
4	75	35.89	1.25	3.5%	1.46	4.1%	3.26	9.1%	3.78	10.5%
5	75	55.66	2.28	4.1%	1.92	3.5%	4.78	8.6%	5.64	10.1%
6	75	82.78	3.71	4.5%	2.20	2.7%	7.25	8.8%	8.44	10.2%

Reproducibility between lots

Seven samples for aCL IgG and aβ2GPI IgG and six samples for aCL IgM and aβ2GPI IgM 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 tables below.

aCL IgG			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	1.61	0.08	5.2%	0.07	4.4%	0.12	7.2%	0.16	9.9%
2	75	4.16	0.21	5.0%	0.18	4.3%	0.19	4.6%	0.34	8.1%
3	75	19.71	0.98	5.0%	0.99	5.0%	2.17	11.0%	2.58	13.1%
4	75	51.11	2.67	5.2%	1.63	3.2%	6.06	11.9%	6.82	13.3%
5	75	124.49	5.93	4.8%	5.92	4.8%	0.00	0.0%	8.37	6.7%
6	75	168.77	7.11	4.2%	8.61	5.1%	0.00	0.0%	11.17	6.6%
7	75	285.27	10.73	3.8%	5.73	2.0%	11.38	4.0%	16.66	5.8%

aβ2GPI IgG			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	0.10	5.0%	0.13	6.7%	0.03	1.7%	0.17	8.5%
2	75	4.94	0.26	5.3%	0.35	7.2%	0.40	8.2%	0.60	12.1%
3	75	23.39	1.08	4.6%	1.24	5.3%	1.10	4.7%	1.98	8.5%
4	75	58.42	3.18	5.5%	2.47	4.2%	3.87	6.6%	5.59	9.6%
5	75	100.56	5.55	5.5%	6.40	6.4%	5.21	5.2%	9.94	9.9%
6	75	144.20	6.89	4.8%	9.57	6.6%	10.69	7.4%	15.92	11.0%
7	75	213.10	8.78	4.1%	5.46	2.6%	21.18	9.9%	23.57	11.1%

aCL IgM			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	2.07	0.07	3.3%	0.10	4.9%	0.03	1.7%	0.13	6.1%
2	75	4.39	0.12	2.8%	0.19	4.3%	0.20	4.6%	0.30	6.9%
3	75	5.25	0.15	2.9%	0.24	4.5%	0.24	4.5%	0.36	6.9%
4	75	31.61	0.83	2.6%	0.85	2.7%	2.16	6.8%	2.46	7.8%
5	75	50.07	1.54	3.1%	1.89	3.8%	5.18	10.3%	5.72	11.4%
6	75	88.20	3.24	3.7%	3.80	4.3%	8.10	9.2%	9.51	10.8%

aβ2GPI IgM			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	1.57	0.05	3.3%	0.09	5.6%	0.06	4.0%	0.12	7.6%
2	75	4.62	0.15	3.2%	0.25	5.4%	0.15	3.3%	0.33	7.0%
3	75	5.73	0.20	3.5%	0.28	4.8%	0.00	0.0%	0.34	6.0%
4	75	24.76	0.61	2.5%	0.68	2.7%	1.86	7.5%	2.07	8.4%
5	75	54.40	1.63	3.0%	2.45	4.5%	4.54	8.3%	5.41	9.9%
6	75	80.53	2.52	3.1%	3.27	4.1%	7.35	9.1%	8.43	10.5%

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

The LoB, LoD, and LoQ of the aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays in the Aptiva APS IgG and Aptiva APS IgM 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 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 IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays (all having a p-value = <0.0001)

The aCL IgG LoB for both reagent lots was determined as 0.00 FLU. The final LoB value for aCL IgG is 0.00 FLU.

The aβ2GPI IgG LoB for one reagent lot was determined as 0.00 FLU, and for the second reagent lot as 0.02 FLU. The final LoB value for aβ2GPI IgG is 0.02 FLU.

The aCL IgM LoB for one reagent lot was determined as 0.01 FLU, and for the second reagent lot as 0.00 FLU. The final LoB value for aCL IgM is 0.01 FLU.

The aβ2GPI IgM LoB for one reagent lot was determined as 0.03 FLU, and for the second reagent lot as 0.02 FLU. The final LoB value for aβB2GPI IgM is 0.03 FLU.

Study protocol for LoD:
Four low level samples for aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM 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 assay, on each reagent lot. The LoD was determined separately for each assay, on each reagent lot.

The aCL IgG limit of detection for one reagent lot was determined as 0.07 FLU, and for the second reagent lot as 0.07 FLU. The final LoD value for aCL IgG is 0.07 FLU.

The aβ2GPI IgG limit of detection for one reagent lot was determined as 0.07 FLU, and for the second reagent lot as 0.09 FLU. The final LoD value for aβ2GPI IgG is 0.09 FLU.

The aCL IgM limit of detection for one reagent lot was determined as 0.04 FLU, and for the second reagent lot as 0.03 FLU. The final LoD value for aCL IgM is 0.04 FLU.

The aβ2GPI IgM limit of detection for one reagent lot was determined as 0.06 FLU, and for the second reagent lot as 0.06 FLU. The final LoD value for aβ2GPI IgM is 0.06 FLU.

Study protocol for LoQ:
Four low level samples for aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM 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 assay, on each reagent lot. The LoQ was determined separately for each assay, on each reagent lot. The LoQ was determined in each case by calculating the total imprecision of each.

The aCL IgG limit of quantitation for one reagent lot was determined as 0.25 FLU, and for the second reagent lot as 0.29 FLU. The final LoQ value is 0.29 FLU, which has been set as the lower limit of the analytical measuring range of the aCL IgG assay.

The aβ2GPI IgG limit of quantitation for one reagent lot was determined as 0.21 FLU, and for the second reagent lot as 0.21 FLU. The final LoQ value is 0.21 FLU, which has been set as the lower limit of the analytical measuring range of the aβ2GPI IgG assay.

The aCL IgM limit of quantitation for one reagent lot was determined as 0.06 FLU, and for the second reagent lot as 0.04 FLU. The final LoQ value is 0.06 FLU. The lower limit of the analytical measuring range of the aCL IgM assay has been set at 0.10 FLU.

The aβ2GPI IgM limit of quantitation for one reagent lot was determined as 0.09 FLU, and for the second reagent lot as 0.09 FLU. The final LoQ value is 0.09 FLU. The lower limit of the analytical measuring range of the aβ2GPI IgM assay has been set at 0.10 FLU.

Analytical Measuring Range (AMR)

Within the Aptiva APG IgG Reagent:

aCL IgG:	0.29 – 328.94 FLU
aβ2GPI IgG:	0.21 – 256.70 FLU

Within the Aptiva APG IgM Reagent:

aCL IgM:	0.10 – 114.68 FLU
aβ2GPI IgM:	0.10 – 95.86 FLU

High concentration hook effect

To assess hook effect, 2 samples aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays were tested at increasing 2-fold serial dilutions from the standard 1:8 dilution used by the Aptiva APS IgG and Aptiva APS IgM Reagents. All FLU values above the analytical measuring ranges of the two assays are theoretical and were mathematically calculated using the 4 parameters of their respective calibration curves. All samples showed increase in FLU values as dilution factor became more concentrated; thereby, confirming that high positive specimens above the AMR do not show hook effect up to 2645.36 FLU for aCL IgG, 1790.48 FLU for aβ2GPI IgG, 167.25 FLU for aCL IgM and 126.13 FLU for the aβ2GPI IgM (theoretical values calculated) in the Aptiva APS IgG and Aptiva APS IgM Reagents.

Linearity

The Linearity of the AMR was calculated separately for aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays as part of the Aptiva APS IgG and Aptiva APS IgM Reagents.

The linearity of the AMR of Aptiva APS IgM and Aptiva APS IgG was evaluated by a study according to CLSI EP06, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline. Five human serum samples for Aptiva APS IgG and four human serum samples for Aptiva APS IgM 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 IgG:

Sample	Test Range in FLU	Slope (95% CI)	R^2	Range of Linearity Deviations
1	38.22 – 382.20	1.00 (0.96 to 1.03)	0.99	-11.2% to 7.4%
2	9.35 – 46.74	1.00 (0.97 to 1.04)	0.99	-7.2% to 6.6%
3	1.62 – 16.19	0.99 (0.96 to 1.02)	1.00	-13.1% to 2.6%
4	0.96 – 4.79	0.98 (0.94 to 1.02)	0.99	-12.9% to 5.7% or -0.24 FLU
5	0.11 - 1.09	1.00 (0.95 to 1.04)	0.98	-10.3% to 13.5%

aβ2GPI IgG:

Sample	Test Range in FLU	Slope (95% CI)	R^2	Range of Linearity Deviations
1	30.12 – 301.21	1.00 (0.96 to 1.04)	0.99	-12.1% to 11.6%
2	7.13 – 35.67	1.00 (0.96 to 1.04)	0.98	-6.9% to 12.3%
3	1.45 – 14.55	0.99 (0.95 to 1.02)	0.99	-11.7% to 13.5% or 0.45 FLU
4	0.39 – 3.87	0.91 (0.83 to 0.99)	0.99	-2.1% to 10.1% or -0.46 to -0.17 FLU
5	0.11 – 1.09	1.00 (0.95 to 1.04)	0.98	-10.3% to 13.5%

These data demonstrate the linearity of the analytical measuring range (0.29 – 328.94 FLU) of the aCL IgG assay and the analytical measuring range (0.21 – 256.70 FLU) of the aβ2GPI IgG assay, both as part of the Aptiva APS IgG Reagent.

aCL IgM:

Sample	Test Range in FLU	Slope (95% CI)	R^2	Range of Linearity Deviations
1	11.81 – 118.12	1.06 (1.02 to 1.11)	0.99	-6.1% to 11.5%
2	1.80 – 18.00	1.03 (1.01 to 1.05)	1.00	-2.7% to 8.8% or 0.57 FLU
3	0.23 – 2.28	1.01 (0.99 to 1.04)	1.00	-9.7% to 5.8%
4	0.04 – 0.37	1.07 (1.02 to 1.12)	0.99	-6.8% to 14.7% or 0.01 to 0.02 FLU

aβ2GPI IgM:

Sample	Test Range in FLU	Slope (95% CI)	R^2	Range of Linearity Deviations
1	10.21 – 102.10	1.07 (1.02 to 1.13)	0.99	-7.7% to 13.5%
2	1.50 – 15.04	1.06 (1.03 to 1.09)	0.99	-5.8% to 12.6%
3	0.17 – 1.75	1.01 (0.97 to 1.05)	0.99	-10.8% to 9.9% or -0.06 FLU
4	0.04 – 0.37	1.06 (0.99 to 0.13)	0.99	-5.6% to 9.7% or 0.02 to 0.03 FLU

These data demonstrate the linearity of the analytical measuring range (0.10 – 114.68 FLU) of the aCL IgM assay and the analytical measuring range (0.10 – 95.86 FLU) of the aβ2GPI IgM assay, both as part of the Aptiva APS IgM Reagent.

Interference

The interference study was performed according to CLSI EP07-A2, Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition. Six human specimens, a set of three human serum samples (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, and acetaminophen) were spiked into each specimen and the resulting samples were assessed in five replicates with the aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays as part of the Aptiva APS IgG and Aptiva APS IgM Reagents assays. Recovery of the unit values was calculated compared to control samples.

No interference was detected for aCL IgG and aβ2GPI IgG with bilirubin at 1.0 mg/mL, hemoglobin at 10.0 g/L, triglycerides at 1000.0 mg/dL, cholesterol at 332.5 mg/dL, RF IgM at 153.4 IU/mL, human IgG at 70 mg/mL, ibuprofen at 21.9 mg/dL, warfarin at 7.5 mg/dL, prednisone at 0.0099 mg/mL acetaminophen at 15.6 mg/dL, aspirin at 3 mg/dL, hydroxychloroquine at 0.465 mg/dL, omeprazole at 0.840 mg/dL, simvastatin at 0.168 mg/dL and heparin at 330 units/dL.

Aptiva APS IgG (aCL IgG)		**Percent Recovery or FLU Difference**		
Endogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Bilirubin, Conjugated	1.0 mg/mL	99.8%	105.4%	104.1%
Hemoglobin	10.00 g/L	98.8%	106.7%	114.0%
Triglyceride	1000.0 mg/dL	99.5%	94.0%	95.2%
Cholesterol	332.5 mg/dL	0.39 FLU	105.3%	102.5%
RF IgM	153.4 IU/mL	103.8%	108.7%	100.9%
Human IgG	20.0 mg/mL	0.41 FLU	108.9%	101.1%
Exogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Ibuprofen	21.9 mg/dL	97.7%	105.0%	97.1%
Warfarin	7.5 mg/dL	95.9%	102.3%	98.8%
Prednisone	0.0099 mg/dL	94.4%	96.4%	99.8%
Acetaminophen	15.6 mg/dL	98.7%	107.8%	101.0%
Aspirin	3.00 mg/dL	95.4%	97.8%	100.8%
Hydroxychloroquine	0.465 mg/dL	98.2%	102.8%	96.6%
Omeprazole	0.840 mg/dL	97.8%	86.6%	90.4%
Simvastatin	0.168 mg/dL	106.4%	104.3%	102.1%
Heparin	330 units/dL	101.5%	113.3%	101.9%

Aptiva APS IgG (aβ2GPI IgG)		**Percent Recovery or FLU Difference**		
Endogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Bilirubin, Conjugated	1.0 mg/mL	99.5%	107.7%	104.3%

Aptiva APS IgG (aβ2GPI IgG)		**Percent Recovery or FLU Difference**		
Hemoglobin	10.00 g/L	104.9%	106.7%	111.6%
Triglyceride	1000.0 mg/dL	99.3%	92.1%	94.4%
Cholesterol	332.5 mg/dL	0.28 FLU	102.1%	99.7%
RF IgM	153.4 IU/mL	102.1%	108.8%	100.7%
Human IgG	20.0 mg/mL	0.18 FLU	104.7%	97.4%
Exogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Ibuprofen	21.9 mg/dL	101.1%	102.5%	99.2%
Warfarin	7.5 mg/dL	100.7%	99.3%	102.8%
Prednisone	0.0099 mg/dL	97.6%	95.2%	103.7%
Acetaminophen	15.6 mg/dL	87.0%	103.8%	106.4%
Aspirin	3.00 mg/dL	98.3%	98.3%	100.6%
Hydroxychloroquine	0.465 mg/dL	88.3%	97.9%	93.7%
Omeprazole	0.840 mg/dL	88.3%	85.7%	88.6%
Simvastatin	0.168 mg/dL	96.1%	99.5%	98.4%
Heparin	330 units/dL	113.8%	102.0%	102.7%

No interference was detected for aCL IgM and aβ2GPI IgM with bilirubin at 1.0 mg/mL, hemoglobin at 10.0 mg/mL, triglycerides at 1000.0 mg/dL, cholesterol at 332.5 mg/dL, RF IgM at 153.4 IU/mL, human IgG at 70 mg/mL, ibuprofen at 21.9 mg/dL, warfarin at 7.5 mg/dL, prednisone at 0.0099 mg/mL acetaminophen at 15.6 mg/dL, aspirin at 3 mg/dL, hydroxychloroquine at 0.465 mg/dL, omeprazole at 0.840 mg/dL, simvastatin at 0.168 mg/dL and heparin at 330 units/dL.

Aptiva APS IgM (aCL IgM)		**Percent Recovery or FLU Difference**		
Endogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Bilirubin, Conjugated	1.0 mg/mL	105.8%	101.7%	102.3%
Hemoglobin	10.00 g/L	109.4%	105.9%	98.0%
Triglyceride	1000.0 mg/dL	97.6%	99.2%	100.9%
Cholesterol	332.5 mg/dL	106.0%	104.4%	101.2%
RF IgM	153.4 IU/mL	98.3%	100.1%	96.5%
Human IgG	70.0 mg/mL	96.0%	98.2%	96.6%
Exogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Ibuprofen	21.9 mg/dL	99.5%	100.1%	99.7%
Warfarin	7.5 mg/dL	99.4%	97.1%	100.9%
Prednisone	0.0099 mg/dL	99.7%	102.0%	97.3%
Acetaminophen	15.6 mg/dL	98.9%	97.5%	100.5%
Aspirin	3.00 mg/dL	98.5%	103.9%	102.5%
Hydroxychloroquine	0.465 mg/dL	94.1%	98.2%	101.9%
Omeprazole	0.840 mg/dL	118.4%	90.2%	93.3%
Simvastatin	0.168 mg/dL	84.4%	89.7%	98.6%
Heparin	330 units/dL	108.1%	102.6%	114.4%

Aptiva APS IgM (aβ2GPI IgM)		Percent Recovery or FLU Difference		
Endogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Bilirubin, Conjugated	1.0 mg/mL	104.2%	99.7%	102.6%
Hemoglobin	10.00 g/L	108.8%	108.1%	98.1%
Triglyceride	1000.0 mg/dL	95.4%	103.0%	102.3%
Cholesterol	332.5 mg/dL	102.1%	101.3%	102.7%
RF IgM	153.4 IU/mL	101.9%	97.7%	97.7%
Human IgG	70.0 mg/mL	97.5%	98.8%	97.9%
Exogenous Interfering substance	Final Conc.	Negative	Cutoff	Positive
Ibuprofen	21.9 mg/dL	98.5%	100.0%	100.7%
Warfarin	7.5 mg/dL	95.5%	99.6%	99.7%
Prednisone	0.0099 mg/dL	98.4%	106.0%	96.9%
Acetaminophen	15.6 mg/dL	100.1%	102.3%	101.1%
Aspirin	3.00 mg/dL	96.9%	102.2%	103.6%
Hydroxychloroquine	0.465 mg/dL	95.6%	96.3%	102.4%
Omeprazole	0.840 mg/dL	0.27 FLU	91.8%	97.2%
Simvastatin	0.168 mg/dL	86.1%	93.4%	102.6%
Heparin	330 units/dL	111.5%	109.0%	112.6%

Sample Stability and Handling

For the aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays, five 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 21 days while stored at 2-8°C, up to 49 hours while stored at room temperature (20-26°C), and after repeated freeze/thaw cycles up to 6 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 5 freeze/thaw cycles.

Reagent Stability

Shelf life

Real-time stability (on-going) and accelerated stability studies were performed to establish the initial claim for shelf life for the Aptiva APS IgG and the Aptiva APS IgM Reagents, 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.

A shelf-life of nine months was assigned to the Aptiva APS IgG Reagent and seven months was assigned to the Aptiva APS IgM Reagent.

Real time stability

Real-time stability testing has been scheduled on the Aptiva APS IgA Reagent and Aptiva APS IgM Regents, 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 IgG and Aptiva APS IgM reagents, one lot of reagents was tested using 11 samples (with different reactivity levels) for IgG and seven samples (with different reactivity levels) for IgM. The specimens were tested periodically for 33 days for IgG and 37 days for IgM. On day 14 the reagent was recalibrated, and a specific Working Curve was generated. Percent recoveries were calculated compared to the day zero 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 IgG and Aptiva APS IgM Reagents was set at 28 days, with a 14-day recalibration.

Cut-off, reference range

The following cut-off is used for the aCL IgG, aβ2GPI IgG, aCL IgM and aβ2GPI IgM assays in the Aptiva APS IgG and Aptiva APS IgM Reagents:

Negative	<5.00 FLU
Positive	≥5.00 FLU

The reference population for establishing the cutoff values for the aCL IgG and aβ2GPI IgG assays in the Aptiva APS IgG Reagent consisted of 52 apparently healthy subjects and for the aCL IgM and aβ2GPI IgM assays in the Aptiva APS IgM Reagent 54 apparently healthy subjects.

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 99th percentile of the results obtained on the reference healthy population.

For the Aptiva APS IgG Reagent (including the aCL and aβ2GPI assays) based on the distribution of result values of healthy controls and internal APS samples (data not provided), the cutoff was established at 144 MFI for aCL IgG and 256 MFI for aβ2GPI IgG and was assigned a value of 5.00 FLU. With this cutoff, we ensure that the cutoff value is greater than the 99th percentile on reference healthy population (105 MFI and 71 MFI for aCL IgG and for aβ2GPI IgG, respectively).

For the Aptiva APS IgM Reagent (including the aCL and aβ2GPI assays) based on the distribution of result values of healthy controls and internal APS samples (data not provided), the cutoff was established at 564 MFI for aCL IgM and 757 MFI for aβ2GPI IgM and was assigned a value of 5.00 FLU. With this cutoff, we ensure that the cutoff value is greater than the 99th percentile on reference healthy population (195 MFI for aCL IgM and 233 MFI for aβ2GPI IgM).

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 IgG and Aptiva APS IgM Reagents.

For Aptiva APS IgG, a total of 526 characterized samples were included in this validation set, including 60 patients with primary antiphospholipid syndrome and 62 patients with secondary antiphospholipid syndrome (pAPS and sAPS) and 404 control samples from patients with various types of autoimmune and infectious diseases. All samples were run on the Aptiva APS IgG Reagent. The distribution of the cohort

Patient Group	N=526	aCL IgG	aCL IgG
		No. Positive	% Positive
APS combined	**122**	**66**	**54.1%**
pAPS	60	33	55.0%
sAPS	62	33	53.2%
Controls	**404**	**2**	**0.5%**
Infectious Disease	58	0	0.0%
PREPI	37	1	2.7%
SLE no APS	27	0	0.0%
Systemic sclerosis	12	1	8.3%
Crohn's Disease	29	0	0.0%
Ulcerative Colitis (UC)	27	0	0.0%
Rheumatoid Arthritis	21	0	0.0%
Fetal Loss no APS	15	0	0.0%
Thrombosis no APS	4	0	0.0%
ANCA-associated vasculitis (AAV)	15	0	0.0%
Autoimmune Thyroid	30	0	0.0%
Celiac Disease (CD)	30	0	0.0%

Patient Group	N=526	aCL IgG No. Positive	aCL IgG % Positive
COVID-19 related thrombosis	20	0	0.0%
Hematologic malignancies	16	0	0.0%
Idiopathic thrombocytopenic purpura (ITP)	17	0	0.0%
Solid tumor malignancies	16	0	0.0%
Deep vein thrombosis	30	0	0.0%

Patient Group	N=526	aβ2GPI IgG No. Positive	aβ2GPI IgG % Positive
APS combined	**122**	**65**	**53.3%**
pAPS	60	32	53.3%
sAPS	62	33	53.2%
Controls	**404**	**4**	**1.0%**
Infectious Disease	58	0	0.0%
PREPI	37	1	2.7%
SLE no APS	27	0	0.0%
Systemic sclerosis	12	1	8.3%
Crohn's Disease	29	0	0.0%
Ulcerative Colitis (UC)	27	0	0.0%
Rheumatoid Arthritis	21	1	4.8%
Fetal Loss no APS	15	0	0.0%
Thrombosis no APS	4	0	0.0%
ANCA-associated vasculitis (AAV)	15	0	0.0%
Autoimmune Thyroid	30	0	0.0%
Celiac Disease (CD)	30	0	0.0%
COVID-19 related thrombosis	20	1	5.0%
Hematologic malignancies	16	0	0.0%
Idiopathic thrombocytopenic purpura (ITP)	17	0	0.0%
Solid tumor malignancies	16	0	0.0%
Deep vein thrombosis	30	0	0.0%

Clinical sensitivity and specificity for the Aptiva APS IgG (aCL IgG) were analyzed in the table below:

Clinical Analysis (N=526)		Diagnosis		
		APS	Controls or Non-APS	Total
Aptiva APS IgG (aCL IgG)	Positive ≥ 5.00	66	2	68
	Negative < 5.00	56	402	458
	Total	122	404	526

Sensitivity	54.1% (45.3 – 62.7%)
Specificity	99.5% (98.2 – 99.9%)

Clinical sensitivity and specificity for the Aptiva APS IgG (aβ2GPI IgG) were analyzed in the table below:

Clinical Analysis (N=526)		Diagnosis		
		APS	Controls or Non-APS	Total
Aptiva APS IgG (aβ2GPI IgG)	Positive ≥ 5.00	65	4	69
	Negative < 5.00	57	400	457
	Total	122	404	526

Sensitivity	53.3 % (44.5-61.9%)
Specificity	99.0% (97.5-99.6%)

For Aptiva APS IgM, a total of 689 characterized samples were included in this validation set, including 291 samples from APS patients and 398 control samples from patients with various types of autoimmune and infectious diseases. All samples were run on the Aptiva APS IgM Reagent. The distribution of the cohort and the aCL IgM and aβ2GPI IgM positivity rate is in the tables below:

Patient Group	**N=689**	**aCL IgM**	**aCL IgM**
		No. Positive	**% Positive**
APS combined	**291**	**80**	**27.5%**
pAPS	219	60	27.4%
sAPS	72	20	27.8%
Controls	**398**	**10**	**2.5%**
Infectious Disease	69	0	0.0%

Patient Group	N=689	aCL IgM No. Positive	aCL IgM % Positive
Myositis	20	1	5.0%
Autoimmune Thyroiditis	35	3	8.6%
Celiac Disease (CD)	50	0	0.0%
Ulcerative Colitis (UC)	19	1	5.3%
Rheumatoid Arthritis	13	1	7.7%
Atopic Dermatitis	11	0	0.0%
Fetal Loss no APS	27	0	0.0%
Pre-Eclampsia	17	0	0.0%
Thrombosis no APS	7	1	14.3%
ANCA-associated vasculities	15	0	0.0%
COVID-19 related thrombosis	20	1	5.0%
Hematologic malignancies	16	0	0.0%
Solid tumor malignancies	16	1	6.3%
Idiopathic thrombocytopenic purpura (ITP)	17	0	0.0%
Deep vein thrombosis	30	1	3.3%
Other disease controls	16	0	0.0%

Patient Group	N=689	aβ2GPI IgM No. Positive	aβ2GPI IgM % Positive
APS combined	**291**	**72**	**24.7%**
pAPS	219	52	23.7%
sAPS	72	20	27.8%
Controls	**398**	**6**	**1.5%**
Infectious Disease	69	0	0.0%
Myositis	20	0	0.0%
Autoimmune Thyroiditis	35	2	5.7%
Celiac Disease (CD)	50	0	0.0%
Ulcerative Colitis (UC)	19	1	5.3%
Rheumatoid Arthritis	13	1	7.7%
Atopic Dermatitis	11	0	0.0%
Fetal Loss no APS	27	0	0.0%
Pre-Eclampsia	17	0	0.0%
Thrombosis no APS	7	1	14.3%
ANCA-associated vasculities	15	0	0.0%
COVID-19 related thrombosis	20	0	0.0%
Hematologic malignancies	16	0	0.0%
Solid tumor malignancies	16	1	6.3%
Idiopathic thrombocytopenic purpura (ITP)	17	0	0.0%
Deep vein thrombosis	30	0	0.0%
Other disease controls	16	0	0.0%

Clinical sensitivity and specificity for the Aptiva APS IgM (aCL IgM) were analyzed in the table below:

Clinical Analysis (N=689)		Diagnosis		
		APS	Controls or Non-APS	Total
Aptiva APS IgM (aCL IgM)	Positive ≥ 5.00	80	10	90
	Negative < 5.00	211	388	599
	Total	291	398	689

Sensitivity	27.5% (22.7 – 32.9%)
Specificity	97.5% (95.4 – 98.6%)

Clinical sensitivity and specificity for the Aptiva APS IgM (aβ2GPI IgM) a were analyzed in the table below:

Clinical Analysis (N=689)		Diagnosis		
		APS	Controls or Non-APS	Total
Aptiva APS IgM (aβ2GPI IgM)	Positive ≥ 5.00	72	6	78
	Negative < 5.00	219	392	611
	Total	291	398	689

Sensitivity	24.7% (20.1 – 30.0%)
Specificity	98.5% (96.8 – 99.3%)

Expected values

The expected value in the normal population is “negative”. A panel of 200 apparently healthy blood donors (106 females/94 males, ages 18 to 70 years, with an average and median age of 37) were tested on the Aptiva APS IgG and Aptiva APS IgM Reagent.

For Aptiva APS IgG, the aCL IgG with a cut-off of 5.00 FLU, no samples were positive, with a mean concentration of 0.29 FLU, and values ranging from 0.29 to 0.42 FLU. For aβ2GPI IgG, with a cut-off of 5.00 FLU, no samples were positive, with a mean concentration of 0.21 FLU, and values ranging from 0.21 to 0.47 FLU.

For Aptiva APS IgM, the aCL IgM with a cut-off of 5.00 FLU, no samples were positive, with a mean concentration of 0.14 FLU, and values ranging from 0.10 to 2.54 FLU. For aβ2GPI IgM, with a cut-off of 5.00 FLU, no samples were positive, with a mean concentration of 0.15 FLU, and values ranging from 0.10 to 3.11 FLU.

Comparison with predicate device

For Aptiva APS IgG, samples for method comparison analysis included all samples analysis included all samples from the clinical validation study that display results within the analytical measuring range of the assay and its predicate device.

Method comparison of the Aptiva APS IgG (aCL IgG) with the predicate device:

Method Comparison (N=202)		QUANTA Flash aCL IgG			Percent Agreement
		Positive	Negative	Total	(95% Confidence)
Aptiva APS IgG (aCL IgG)	Positive ≥ 5.00	31	7	38	PPA: 81.6% (66.6-90.8%)
	Negative < 5.00	7	157	164	NPA: 95.7% (91.5-97.9%)
	Total	38	164	202	TPA: 93.1% (88.7-95.8%)

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

Method comparison of the Aptiva APS IgG (aβ2GPI IgG) with the predicate device:

Method Comparison (N=108)		QUANTA Lite Beta 2GP1 IgG ELISA			Percent Agreement
		Positive	Negative	Total	(95% Confidence)
Aptiva APS IgG (aβ2GPI IgG)	Positive ≥ 5.00	44	6	50	PPA: 88.0% (76.2-94.4%)
	Negative < 5.00	6	52	58	NPA: 89.7% (79.2-95.2%)
	Total	50	58	108	TPA: 88.9% (81.6-93.5%)

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

For Aptiva APS IgM, samples for method comparison analysis included all samples from the clinical validation study that display results within the analytical measuring range of the assay and its predicate device These samples were tested on both the Aptiva APS IgM Reagent and on their predicate QUANTA Flash aCL IgM and QUANTA Flash β2GP1 IgM Reagents.

Method comparison of the Aptiva APS IgM (aCL IgM) with the predicate device:

Method Comparison (N=422)		QUANTA Flash aCL IgM			Percent Agreement
		Positive	Negative	Total	(95% Confidence)
Aptiva APS IgM (aCL IgM)	Positive ≥ 5.00	40	37	77	PPA: 87.0% (74.3-93.9%)
	Negative < 5.00	6	339	345	NPA: 90.2% (86.7-92.8%)
	Total	46	376	422	TPA: 89.8% (86.6-92.3%)

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

Method comparison of the Aptiva APS IgM (aβ2GPI IgM) with the predicate device:

Method Comparison (N=244)		QUANTA Flash β2GPI IgM			Percent Agreement
		Positive	Negative	Total	(95% Confidence)
Aptiva APS IgM (aβ2GPI IgM)	Positive ≥ 5.00	24	34	58	PPA: 88.9% (71.9-96.1%)
	Negative < 5.00	3	183	186	NPA: 84.3% (78.9-88.6%)
	Total	27	217	244	TPA: 84.8% (79.8-88.8%)

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