

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION MEMORANDUM**

A. 510(k) Number:

K143754

B. Purpose for Submission:

New Device

C. Measurand:

Anti-cyclic citrullinated peptide 3 (CCP3) IgG autoantibodies

D. Type of Test:

Semi-quantitative chemiluminescent immunoassay (CIA)

E. Applicant:

INOVA Diagnostics, Inc.

F. Proprietary and Established Names:

QUANTA Flash® CCP3
QUANTA Flash® CCP3 Calibrators
QUANTA Flash® CCP3 Controls

G. Regulatory Information:

1. Regulation section:

21 CFR §866.5775 – Rheumatoid Factor Immunological Test System
21 CFR §862.1150 – Calibrator
21 CFR §862.1660 – Quality Control Material (Assayed and Unassayed)

2. Classification:

Class II – Assay and Calibrator
Class I – Control

3. Product code:

NHX – Antibodies, Anti-Cyclic Citrullinated Peptide (CCP)
JIT – Calibrator, Secondary

JJX – Single (Specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

Immunology (82) (Assay)

Clinical Chemistry (75) (Calibrators and Controls)

H. Intended Use:

1. Intended use(s):

QUANTA Flash CCP3 is a chemiluminescent immunoassay for the semi-quantitative determination of IgG anti-CCP3 antibodies in human serum. The presence of anti-CCP3 antibodies, in conjunction with clinical findings and other laboratory tests, is an aid in the diagnosis of rheumatoid arthritis.

QUANTA Flash® CCP3 Calibrators are intended for use with the QUANTA Flash® CCP3 chemiluminescent immunoassay for the determination of IgG anti-CCP3 antibodies in human serum. Each calibrator establishes a point of reference for the working curve that is used to calculate unit values.

QUANTA Flash® CCP3 Controls are intended for use with the QUANTA Flash® CCP3 chemiluminescent immunoassay for quality control in the determination of IgG anti-CCP3 antibodies in human serum.

2. Indication(s) for use:

Same as Intended Use above

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

BIO-FLASH® chemiluminescent analyzer (k083518)

I. Device Description:

The QUANTA Flash® CCP3 contains one QUANTA Flash® CCP3 reagent cartridge, one vial of resuspension buffer, and one transfer pipette.

The QUANTA Flash® CCP3 reagent cartridge contains the following reagents for 100 determinations:

- a. CCP3 coated paramagnetic beads, lyophilized
- b. Assay buffer
- c. Tracer IgG – Isoluminol labeled anti-human IgG antibodies in buffer.

The QUANTA Flash® CCP3 Calibrators set is sold separately and contains two vials of Calibrator 1 and two vials of Calibrator 2:

- a. Calibrator 1: Two barcode labeled tubes containing 0.7 mL prediluted, ready to use reagent. Calibrator 1 contains human antibodies to CCP3 in stabilizer and preservative.
- b. Calibrator 2: Two barcode labeled tubes containing 0.7 mL prediluted, ready to use reagent. Calibrator 2 contains human antibodies to CCP3 in stabilizer and preservative.

The QUANTA Flash® CCP3 Controls kit contains two vials of Negative Control and two vials of Positive Control:

- a. Negative Control: Two barcode labeled tubes containing 0.5 mL, ready to use reagent. Negative control contains human antibodies to CCP3 in and preservative.
- b. Positive Control: Two barcode labeled tubes containing 0.5 mL, ready to use reagent. Positive control contains human antibodies to CCP3 in stabilizer and preservative.

J. Substantial Equivalence Information:

- 1. Predicate device name(s) and 510(k) number(s):

QUANTA Lite® CCP3 IgG ELISA, k052264

- 2. Comparison with predicate:

Similarities		
Item	Device QUANTA Flash® CCP3	Predicate QUANTA Lite® CCP3
Intended Use	Semi-quantitative determination of anti-CCP3 antibodies in human serum. An aid in the diagnosis of rheumatoid arthritis (RA).	Same
Antigen	Synthetic peptide	Same
Analyte	Anti-CCP3 IgG antibodies	Same
Shelf Life	One year at 2–8°C	Same

Differences		
Item	Device: QUANTA Flash® CCP3	Predicate: QUANTA Lite® CCP3
Detection	Chemiluminescent immunoassay	Enzyme-linked immunosorbent assay
Solid Phase	Paramagnetic microparticles (beads)	96-well plate
Sample Type	Serum	Serum, citrated and EDTA plasma
Conjugate	Isoluminol conjugated anti-human IgG	HRP conjugated anti-human IgG
Control	Negative and Positive	Negative, Low positive and High positive
Cut-off	Negative: <20 CU Positive: ≥20 CU	Negative: <20 Unit Weak positive: 20–39 Unit Moderate positive: 40–59 Unit Strong positive: ≥60 Unit
Assay Measuring Range (AMR)	4.6–2776.8 CU	No claim of the reportable range

QUANTA Flash® CCP3 Calibrators

Similarities		
Item	Device QUANTA Flash® CCP3 Calibrators	Predicate
Intended Use	For use with QUANTA Flash® CCP3 reagents. Each calibrator establishes a point of reference for the working curve that is used to calculate unit values.	No separate intended use; calibrator is part of the kit
Analyte	Anti-CCP3 antibodies	Same
Calibration	Lot specific Master Curve + two Calibrators (sold separately)	CCP3 ELISA Low Positive, and Calibrators A–E (included in the kit)
Matrix	Human serum, buffers, stabilizers and preservative	Same
Physico-chemical characteristics	Liquid, prediluted, ready to use	Same
Shelf Life/Storage	One year at 2–8°C	Same

Differences		
Item	Device QUANTA Flash® CCP3 Calibrators	Predicate
Method	QUANTA Flash® CCP3	QUANTA Lite® CCP3

Differences		
Item	Device QUANTA Flash® CCP3 Calibrators	Predicate
	chemiluminescent immunoassay	ELISA
Unit	CU (chemiluminescent units)	Units

QUANTA Flash® CCP3 Controls

Similarities		
Item	Device QUANTA Flash® CCP3 Controls	Predicate
Intended Use	QUANTA Flash® CCP3 Controls are intended for use with the QUANTA Flash® CCP3 reagents for quality control in the determination of IgG anti-CCP3 autoantibodies in human serum.	No separate intended use; controls are part of the kit.
Analyte	Anti-CCP3 antibodies	Same
Physico- chemical characteristics	Liquid, ready to use	Same
Levels	2 (negative and positive)	Same
Shelf Life/Storage	One year at 2–8°C	Same

Differences		
Item	Device QUANTA Flash® CCP3 Controls	Predicate
Matrix	Human serum, stabilizer, and preservative	Human serum, buffer, stabilizer, and preservative
Unit	CU (chemiluminescent units) (arbitrary)	Units (arbitrary)

K. Standard/Guidance Document Referenced (if applicable):

EP05-A2, Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline, Second Edition.

EP06-A, Evaluation of Linearity of Quantitative Measurement, Approved Guideline, Second Edition.

EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline, Second Edition

EP09-A3, Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline, Second Edition (Interim Revision).

EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline, Second Edition

C28-A3, Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline, Third Addition

L. Test Principle:

The QUANTA Flash® CCP3 assay is a microparticle chemiluminescent immunoassay designed for use on the BIO-FLASH instrument. The instrument platform is a fully automated closed system with continuous load and random access capabilities that automatically processes the samples, runs the assay and reports the results. It includes liquid handling hardware, luminometer and computer with software-user interface. The QUANTA Flash® CCP3 assay utilizes a reagent cartridge format, which is compatible with the BIO-FLASH instrument.

Synthetic cyclic citrullinated peptide is coated onto paramagnetic beads. The bead suspension is lyophilized and stored in the bead tube. Prior to use in the BIO-FLASH system, the sealed reagent tubes are pierced with the reagent cartridge lid and the beads are rehydrated and resuspended using resuspension buffer by pipetting up and down with a transfer pipette. The reagent cartridge is then loaded onto the BIO-FLASH instrument. Samples are also loaded onto the instrument in sample racks. A patient serum sample is prediluted by the BIO-FLASH with system rinse in a small disposable plastic cuvette. Small amounts of the diluted patient serum, the beads, and assay buffer are all combined into a second cuvette, and mixed. This cuvette is then incubated at 37°C. The beads are magnetized and washed several times. Isoluminol conjugated anti-human IgG antibodies are then added to the cuvette, and again incubated at 37°C. The beads are magnetized and washed repeatedly. The isoluminol conjugate is oxidized when Trigger 1 (Fe(III) coproporphyrin in sodium hydroxide solution) and Trigger 2 (urea-hydrogen peroxide in sodium chloride solution) are added to the cuvette, and the flash of light produced from this reaction is measured as Relative Light Units (RLU) by the BIO-FLASH optical system. The RLU are proportional to the amount of isoluminol conjugate that is bound to the human IgG, which is in turn proportional to the amount of anti-CCP3 antibodies bound to the corresponding beads.

For quantitation, the QUANTA Flash® CCP3 assay utilizes a predefined lot specific Master Curve that is uploaded onto the instrument through the reagent cartridge barcode. Every new lot number of reagent cartridge must be calibrated before first use, with the QUANTA Flash® CCP3 Calibrators. Based on the results obtained with the two Calibrators included in the Calibrator Set (sold separately), an instrument specific Working Curve is created, which is used to calculate chemiluminescent units (CU) from the instrument signal (RLU) obtained for each sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision: The precision of the QUANTA Flash® CCP3 assay was evaluated by testing eight serum samples containing various concentrations of anti-CCP3 antibody. Each sample was run in duplicate, twice a day, for 20 days with one reagent lot (total of 80 replicates per sample). All %CV values were within the sponsor's pre-

determined acceptance limit (<10%). The results are summarized in the table below.

Sample	Mean (CU)	Within-Run		Between-Run		Between-Day		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
1	11.7	0.7	5.8	0.0	0.0	0.4	3.5	0.8	6.8
2	21.3	1.0	4.6	0.7	3.2	0.7	3.5	1.4	6.6
3	21.4	0.8	3.6	0.6	2.8	0.9	4.1	1.3	6.1
4	23.0	1.0	4.4	0.0	0.0	0.6	2.8	1.2	5.2
5	55.9	1.4	2.6	1.1	1.9	2.1	3.8	2.8	5.0
6	195.1	8.8	4.5	6.0	3.1	1.3	0.6	10.7	5.5
7	1155.3	56.2	4.9	20.3	1.8	32.6	2.8	68.0	5.9
8	2210.3	119.9	5.4	42.3	1.9	36.6	1.7	132.3	6.0

Reproducibility: A total of eight samples were tested at three sites with one reagent lot to evaluate site-to-site reproducibility. Three samples were run in quadruplicate, twice a day, for five days, to generate 40 data points for each sample at each site. An additional five samples were tested in replicates of five, once a day, for five days, to generate 25 data points for each sample at each site. Data were analyzed for within-run, between-run, between site and total precision. The results are summarized in the table below. All %CV values were within the sponsor's pre-determined acceptance limit (<10%).

Sample	N	Mean (CU)	Within-Run		Between-Run		Between Sites		Total	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
1	120	9.3	0.5	5.2	0.2	2.0	0.0	0.0	0.5	5.6
2	120	35.1	1.6	4.5	0.6	1.6	1.1	3.0	2.0	5.6
3	120	207.9	9.1	4.4	2.3	1.1	4.1	2.0	10.3	4.9
4	75	16.0	0.6	3.5	0.6	3.9	0.5	3.2	1.0	6.2
5	75	24.4	0.6	2.5	0.8	3.3	0.5	1.9	1.1	4.6
6	75	767.5	21.0	2.7	42.3	5.5	11.5	1.5	48.6	6.3
7	75	1447.6	49.8	3.4	65.2	4.5	38.2	2.6	90.5	6.4
8	75	2274.4	102.8	4.5	122.7	5.4	0.0	0.0	160.1	7.0

To evaluate lot-to-lot reproducibility, five samples with anti-CCP3 antibody concentration at various levels across the measuring range (16.2, 24.9, 77.5, 341.1, and 1528.7 CU) were tested. Each sample was tested in replicates of five, one run per day for five days using three difference reagent lots. Mean and %CV for each sample were calculated and %CV values were from 2.8% to 4.0% for all samples.

b. Linearity/assay reportable range:

Linearity: The analytical measuring range of the assay is defined by the lowest and

highest points on the master curve (4.6–2776.8 CU). The linearity across this range was evaluated by a study according to CLSI EP6-A. Serially diluted samples with CCP3 concentrations ranging from 3.5 to 3164.9 CU were prepared by diluting each of five high positive serum samples with negative serum in 10% increments. Each dilution was tested in duplicate. Percentage recovery of obtained mean results was calculated compared to the expected results and the linear regression analysis was performed using the samples falling within the master curve. The results are summarized as follows:

Sample	Test Range(CU)	Slope (95% CI)	Y-intercept (95% CI)	R ²	% Recovery
1	346.5–2772.3	1.00 (0.98–1.02)	0.0 (-36.9–36.9)	1.00	100–109%
2	203.0–2030.0	0.99 (0.96–1.03)	-45.56 (-90.64– -0.48)	0.99	90–100%
3	70.5–705.4	1.00 (0.95–1.04)	22.29 (2.58–41.99)	0.99	100–117%
4	13.5–134.5	0.94 (0.88–1.00)	-2.18 (-7.33–2.97)	0.98	84–104%
5	7.0–34.9	0.97 (0.93–1.02)	0.51 (-0.51–1.53)	0.99	95–104%
All samples	7.0–2772.3	1.07 (1.05–1.10)	-13.84 (-37.21–9.54)	0.99	84–117%

Auto-rerun: To validate the auto-rerun function with 1:20 dilution, four high positive specimens with anti-CCP3 antibody concentration above the assay measuring range (7401.5, 3641.7, 6391.1, and 7859.8 CU) were run with the auto-rerun function enabled on the BIO-FLASH. The same set of samples prepared manually with 1:20 fold dilution was used as reference and tested with the concentration of 7192.9, 3953.1, 6325.1, and 7694.9 CU, respectively. The % recovery values for results obtained with the auto-rerun results compared to results with manual dilution were between 97% and 109%.

Hook effect: The same set of four high positive samples used in the validation study for auto-rerun function and having anti-CCP3 antibody concentration above assay measuring range was examined to assess hook effect. No hook effect was observed up to 7695 CU.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability: There is no recognized standard or reference material for anti-CCP3 antibodies.

Value assignment: The QUANTA Flash® CCP3 Calibrators and Controls are manufactured by diluting human serum that contains high titer of anti-CCP3 antibodies with stabilizer and preservative. The target CU is achieved through trial

dilutions on small scale. Once a dilution is selected, the Calibrators and Controls are bulked, tested, and adjusted. Upon completion of the manufacturing process, the Calibrators and Controls are tested on at least two instruments, on at least two lots of reagent cartridge, in replicates of 10 to determine final value assignment. The target values and ranges for the Calibrators and Controls are listed below:

	Target Value (CU)	Target Range (CU)
<i>QUANTA Flash® CCP3 Calibrators</i>		
Calibrator 1	14	10–16
Calibrator 2	300	270–330
<i>QUANTA Flash® CCP3 Controls</i>		
Negative control	10	8–12
Positive control	50	40–60

Stability:

Kit stability (unopened): The accelerated stability study was performed using three lots of CCP3 coupled beads, calibrators and controls. Real-time stability is on-going. The results to date support a claim of 12 months stability for unopened kit, calibrators and controls stored at 2–8°C.

On-board (In-use) stability: On-board stability study was performed for calibrators, controls and reagent cartridge:

- i. Calibrators: Calibrators were placed uncapped on the instrument, and calibration was performed five times over 8.5 hours. Controls and a panel of characterized patient specimens were run on each calibration curve. Each calibrator is measured in triplicate during calibration.
- ii. Controls: Two vials of each control were assayed twice a day for a total of 20 runs. The first run was used to establish baseline value, and then an additional 19 runs were performed. During runs, the Controls were left uncapped onboard the instrument for 15 minutes per run. When not in use, the controls were capped, and stored at 5°C±3°C.
- iii. Reagent Cartridge: Three lots of cartridges were tested with six serum specimens (with different reactivity levels) along with the Negative and Positive Controls. The specimens were tested periodically up to 90 days. 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.

All results met the manufacturer’s acceptance criteria and support the following stability claim:

Calibrators	8 hours on-board; up to 4 calibrations.
Controls	up to 15 uses with 10 min on-board per use
Reagent Cartridge	60 days on-board

Sample stability: the study was performed with six samples (two negatives, two positives, and two around the cut-off) tested at 2–8°C and room temperature (RT). In addition, the samples were tested for the stability after repeated freeze/thaw cycles up to three cycles. The results support sample stability up to 48 hours of storage at RT, up to 21 days of storage at 2–8°C, and up to three freeze/thaw cycles when samples are stored at or below -20°C.

d. Detection limit:

Limit of Blank (LoB) was determined by assaying four blank samples in five replicates per sample over three days with two reagent lots. Sixty data points per lot were generated. LoB for each lot was calculated separately at the 95th percentile using the non-parametric method, as the dataset showed non-normal distribution. The LoB for two lots was determined to be 410 RLU and 341 RLU. The claimed LoB value is 410 RLU.

The Limit of Detection (LoD) was determined by assaying four samples with low level anti-CCP3 antibody concentration. Each sample was tested in five replicates over three days on two reagent lots. LoD value was calculated as the LoB + 1.645 x SD of the replicates for the low level samples. The LoD of the QUANTA Flash® CCP3 assay for the two lots were determined to be 465 and 478 RLU, which are below the value of the lowest QUANTA Flash® CCP3 Master Curve standard (1600 CU), and therefore below the lower limit of the Analytical Measuring Range of the assay. The claimed LoD is 478 RLU.

e. Analytical specificity:

Endogenous Interference: Three serum samples with antibody concentration at 10.1 CU (negative), 40.5 CU (low positive), and 939.8 CU (high positive) were spiked separately with endogenous interferents. The control samples were prepared for each interfering substance by spiking with the same volume of diluents. Each sample was tested in triplicates and the recovery was calculated by comparing to corresponding control sample. The interferents tested were: bilirubin (10, 5.0 or 2.5 mg/dL), hemoglobin (200, 100, or 50 mg/dL), and triglycerides/cholesterol (1000/224, 500/112 or 250/56 mg/dL). No interference (<15%) was detected in the samples up to the concentrations listed in the table below:

Potential Interfering Substances	Maximum Concentration	Range of % Recovery
Bilirubin	10 mg/dL	101–102%
Hemoglobin	200 mg/dL	97–108%
Triglycerides	1000 mg/dL	98–111%
Cholesterol	224 mg/dL	98–111%

Analytical cross-reactivity: The reference reagent for citrullinated peptide/protein antibodies (ACPA) (P/N IS2723 L/N 08-0202) from the Center of Disease Control and Prevention (CDC) has been tested and showed a concentration of 379.5 CU. Twelve ANA human reference sera from CDC were also tested for the cross reactivity of the QUANTA Flash® CCP3. The sera of CDC9 (human antibodies to Scl-70) showed a concentration of 7.2 CU, and all other reference sera in the panel showed the test results below the lower limit of the measuring range, 4.6 CU.

f. Assay cut-off:

The assay cut-off was determined by testing samples from reference population of 210 subjects (170 apparently healthy blood donors and 40 other control disease samples). The cut-off was established as 20 CU based on the 99th percentile of the results obtained.

	Positive	Negative
QUANTA Flash® CCP3	≥20 CU	<20 CU

2. Comparison studies:

a. Method comparison with predicate device:

Samples for method comparison analysis included 728 samples from the clinical validation study. All these samples were tested on both the QUANTA Flash® CCP3 and the predicate. From the total sample size of 728, results for 420 samples were within the measuring ranges of the assays. The analysis of the results comparing the QUANTA Flash® CCP3 to the predicate is summarized below:

		QUANTA Lite® CCP3 ELISA		
		Positive	Negative	Total
QUANTA Flash® CCP3	Positive	211	19	230
	Negative	13	177	190
	Total	224	196	420

Positive agreement: 94.2% (95% CI: 90.3–96.6%)

Negative agreement: 90.3% (95% CI: 85.4–93.7%)

Overall agreement: 92.4% (95% CI: 89.4–94.6%)

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity and Clinical Specificity:*

A total of 728 patient samples included in the clinical validation for the QUANTA Flash® CCP3. The validation set of samples includes 352 samples from patients diagnosed with RA and 376 samples from patients with other potentially cross-reacting diseases. Clinical sensitivity and specificity to aid in diagnosis of RA are summarized in the following table:

		Clinical Diagnosis of RA		
		Positive	Negative	Total
QUANTA Flash® CCP3	Positive	249	13	262
	Negative	103	363	466
	Total	352	376	728

Clinical Sensitivity: 70.7% (95% CI: 65.8–75.2%)

Clinical Specificity: 96.5% (95% CI: 94.2–98.0%)

The table below shows the results for non-RA samples tested with QUANTA Flash® CCP3:

Non-RA Control Diseases	N	No (%) Positive
Ankylosing Spondylitis	13	0 (0.0%)
Osteoarthritis (NCGN)	49	2 (4.1%)
Polymyalgia Rheumatica	20	2 (10.0%)
Psoriasis Arthritis	14	1 (7.1%)
Systemic Lupus Erythematosus	53	2 (3.8%)
Sjögren's syndrome	20	0 (0%)
Autoimmune hepatitis (AIH)	19	1 (5.3%)
Ulcerative colitis (UC)	11	0 (0%)
Celiac Disease (CD)	20	1 (5.0%)
Lyme Disease	25	0 (0%)
Parvovirus infection	12	0 (0%)
Salmonella infection	10	0 (0%)
HBV	22	0 (0.0%)
HCV	13	0 (0.0%)
Other diseases:	75	4 (5.3%)
Arthritis with colitis ulcerose	1	0 (0.0%)
Arthritis with Crohn's disease	1	1 (100.0%)
Colon Carcinoma	1	0 (6.7%)
Connective Tissue Disease	2	0 (0.0%)

Non-RA Control Diseases	N	No (%) Positive
Cryoglobulinemia	1	0 (0.0%)
Degenerative Spine Disease	6	0 (0.0%)
Fibromyalgia	6	1 (16.7%)
Fibromyalgia, Connective Tissue Disease	1	0 (0.0%)
Fibromyalgia, Osteoarthritis	1	0 (0.0%)
Gout	3	0 (0.0%)
Juvenile Rheumatoid Arthritis	1	0 (0.0%)
Limited Systemic Sclerosis	8	1 (12.5%)
Mixed Connective Tissue Disease	7	0 (0.0%)
Monoarthritis	2	0 (0.0%)
Monoclonal Gammopathy of Unknown Significance (MGUS)	2	0 (0.0%)
Multiple Sclerosis	2	0 (0.0%)
Osteoarthritis, MGUS	1	0 (0.0%)
Osteoarthritis, Osteoarthritis	1	0 (0.0%)
Periarthropathia humeroscapularis	1	0 (0.0%)
Polymyalgia Rheumatica, Temporal Arteritis	1	0 (0.0%)
Polymyositis	2	0 (0.0%)
Primary Biliary Cirrhosis	7	1 (14.3%)
Raynaud-Syndrome	2	0 (0.0%)
Rosacea	1	0 (0.0%)
Sacroiliitis	1	0 (0.0%)
Scoliosis	1	0 (0.0%)
Spondylosis	1	0 (0.0%)
Undifferentiated Connective Tissue Disease	5	0 (0.0%)
Vasculitis	6	0 (0.0%)
Wegener's granulomatosis	1	0 (0.0%)
TOTAL	376	13 (3.5%)

b. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

See assay cut-off.

5. Expected values/Reference range:

The expected value in the normal population is “negative”. Anti-CCP3 antibody levels were analyzed in a cohort of 146 apparently healthy blood donors (66 females and 80 males, ages 17 to 60 years, with an average and median age of 34 years) using the QUANTA Flash® CCP3. The results showed a mean concentration of 5.5 CU with the values ranging from <4.6 to 31.1 CU. Only one sample tested positive (0.7%).

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.