



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY AND INSTRUMENT**

**I Background Information:**

**A 510(k) Number**

K250588

**B Applicant**

Beckman Coulter Inc.

**C Proprietary and Established Names**

Access Rubella IgG

**D Regulatory Information**

Product Code(s)	Classification	Regulation Section	Panel
LFX	Class II	21 CFR 866.3510 - Rubella Virus Serological Reagents	MI - Microbiology

**II Submission/Device Overview:**

**A Purpose for Submission:**

Modification of a previously cleared device, Access Rubella IgG assay to add the DxI 9000 Access Immunoassay Analyzer.

**B Measurand:**

IgG antibodies to Rubella virus.

**C Type of Test:**

Chemiluminescent Immunoassay.

**III Intended Use/Indications for Use:**

**A Intended Use(s):**

See Indications for Use below.

**B Indication(s) for Use:**

The Access Rubella IgG assay is a paramagnetic particle, chemiluminescent immunoassay for the qualitative and quantitative determination of IgG antibodies to the rubella virus in human serum using the Access Immunoassay Systems. The Access Rubella IgG assay aids in the diagnosis of rubella infection and the determination of immunity.

**C Special Conditions for Use Statement(s):**

Rx - For Prescription Use Only

**D Special Instrument Requirements:**

DxI 9000 Access Immunoassay Analyzer.

**IV Device/System Characteristics:**

**A Device Description:**

The Access Rubella IgG assay is a paramagnetic-particle chemiluminescent immunoassay for the qualitative and quantitative detection of Rubella virus-specific IgG antibody in adult human serum using the Access Immunoassay Systems.

The Access Rubella IgG assay consists of the reagent pack, calibrators, and quality controls (QCs) packaged separately. Other items needed to run the assay but not supplied with reagent kit include substrate and wash buffer.

**B Principle of Operation:**

The Access Rubella IgG assay is an enzyme immunoassay using an indirect technique. A sample is added to a reaction vessel with paramagnetic particles coated with Rubella viral membrane antigen. Specific antibodies present in the sample bind to the antigen. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Alkaline phosphatase-conjugated monoclonal anti-human IgG antibody is then added and attaches to the IgG antibodies captured on the particles. A second separation and wash step remove unbound conjugate. Then, the chemiluminescent substrate is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of IgG antibodies to the Rubella virus in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve standardized against the Second International Standard material (2<sup>nd</sup> ISP). Test results are determined automatically by the system software.

The Access Rubella IgG assay results interpretation is as follows:

Results	Result Interpretation	Comments
< 10 IU/mL	Non-reactive	Samples are considered non-reactive for the presence of Rubella IgG antibodies. A non-reactive result may indicate that an individual has not been infected with Rubella or vaccinated and is thus susceptible to infection. A non-reactive result, however, does not rule out an acute infection. If exposure to the pathogen is suspected despite an initial non-reactive result, a second sample should be collected and tested at least two to three weeks later.
$\geq 10$ IU/mL to $< 15$ IU/mL	Equivocal	Samples are considered equivocal for the presence of Rubella IgG antibodies. Specimens that are equivocal may contain low levels of anti-Rubella IgG. As any cutoff is a statistically determined value, it is recommended that results close to the cutoff are interpreted cautiously and further investigated. If exposure to the pathogen is suspected despite an initial equivocal result, a second sample should be collected and tested at least two to three weeks later.
$\geq 15$ IU/mL	Reactive	Samples are considered reactive for the presence of Rubella IgG antibodies and indicate acute or past infection or vaccination.

## C Instrument Description Information:

### 1. Instrument Name:

DxI 9000 Access Immunoassay Analyzer.

### 2. Specimen Identification:

Human serum.

### 3. Specimen Sampling and Handling:

The instrument performs all handling procedures automatically.

### 4. Calibration:

Calibration is required every 28 days. The calibrators are formulated with equine serum and human defibrinated plasma. There is one negative and five positive calibrators containing approximately 10, 25, 50, 200, and 500 IU/mL of human anti-Rubella IgG. They are traceable to the Second International Standard Preparation for Anti-Rubella Serum (2<sup>nd</sup> ISP).

### 5. Quality Control:

Access Rubella IgG Controls are required to run the assay and are available separately. One negative and one positive (target mean of 22 – 43 IU/mL) controls formulated in human defibrinated plasma are traceable to the Second International Standard Preparation for Anti-Rubella Serum (2<sup>nd</sup> ISP).

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

Access Rubella IgG

### B Predicate 510(k) Number(s):

K954687

### C Comparison with Predicate(s):

Device & Predicate Device(s):	Candidate K250588	Predicate K954687
Device Trade Name	Same	Access Rubella IgG
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	The Access Rubella IgG assay is a paramagnetic particle, chemiluminescent immunoassay for the qualitative and quantitative determination of IgG antibodies to the rubella virus in human serum using the Access Immunoassay Systems. The Access Rubella IgG assay aids in the diagnosis of rubella infection and the determination of immunity.
Analyte	Same	IgG antibody to rubella virus
Technology	Same	Two-step immunoenzymatic assay
Format	Same	Chemiluminescent
Method	Same	Automated
Calibration	Same	Utilizes a stored calibration curve
Calibration Frequency	Same	28 days
Sample Type	Same	Serum
Results Interpretation	Same	<10.0 IU/mL: Non-Reactive ≥10 - <15 IU/mL: Equivocal ≥15.0 IU/mL: Reactive
Capture Reagent	Same	Paramagnetic particles coated with rubella (strain HPV 77) sucrose gradient purified antigen
Detection Antibody	Same	Mouse monoclonal anti-human IgG antibody (clone 125 A 15) - alkaline phosphatase (bovine) conjugate

Device & Predicate Device(s):	Candidate K250588	Predicate K954687
Stability	Same	28 days after opening, 2 - 10°C
<b>General Device Characteristic Differences</b>		
Analytical Measuring Interval	5.0 – 500 IU/mL	10.0 – 500 IU/mL
Substrate	Lumi-Phos PRO substrate	Access Substrate
Instrument	DxI 9000 Access Immunoassay Analyzer	Access 2 Immunoassay System

## VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition (Reaffirmed: September 2019).
- CLSI EP06 Evaluation of the Linearity of Quantitative Measurement Procedures - 2nd Edition (2020).
- CLSI EP09c-Ed 3 Measurement Procedure Comparison and Bias Estimation Using Patient Samples (2018).
- CLSI EP12-Ed3 Evaluation of Qualitative, Binary Output Examination Performance, Third Edition (2023).
- CLSI EP17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – 2<sup>nd</sup> Edition (2012).

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

#### 1. Precision/Reproducibility:

- Within-Laboratory Precision:* A 20-day within-laboratory precision study was conducted using 3 DxI 9000 Access Immunoassay Analyzer systems. Six human serum samples were tested in 2 replicates at 2 runs per day over 20 days using 3 reagent lot/calibrator lot combinations, where a unique reagent lot and calibrator lot are paired. The data were analyzed for repeatability (within-run), between-run, between-day, and within-laboratory precision. Within-laboratory precision data summary is shown in Table 1.

**Table 1.** Access Rubella IgG 20-day Within-Laboratory Precision

Sample	n	Mean (IU/mL)	Repeatability (Within-Run)		Between-Run		Between-Day		Between-Instrument/ Reagent Lot/ Calibrator Lot <sup>a</sup>		Overall Precision <sup>b</sup>	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	240	10.6	0.38	3.6	0.29	2.7	0.47	4.4	0.33	3.2	0.75	7.0
Sample 2	240	19.2	0.78	4.0	0.69	3.6	0.91	4.7	0.19	1.0	1.39	7.3
Sample 3	240	59.9	3.09	5.2	2.43	4.0	1.99	3.3	1.10	1.8	4.54	7.6
Sample 4	240	120.7	4.69	3.9	3.89	3.2	6.69	5.5	2.82	2.3	9.48	7.9
Sample 5	240	164.5	5.99	3.6	6.96	4.2	0.00	0.0	1.35	0.8	9.29	5.6
Sample 6	240	379.4	14.36	3.8	8.75	2.3	19.23	5.1	9.75	2.6	27.35	7.2

<sup>a</sup> Access Rubella IgG reagent lot, Access Rubella IgG calibrator lot, and DxI 9000 instrument are confounded, and the confounding effect is represented by Between-Instrument/Reagent Lot/Calibrator Lot.

<sup>b</sup> Overall within-laboratory variability includes within-run, between-run, between-day, and between-instrument/lot variance components.

- b) *Reproducibility (between-Instrument Precision)*: An additional precision study was conducted over 5-day by testing six serum samples on 3 DxI 9000 Access Immunoassay Analyzers in an internal site. The samples were tested with 3 lots of Access Rubella IgG reagents, and 1 lot of Access Rubella IgG calibrator on each instrument with 5 replicates per run and 1 run per day over 5 days. Between-instrument reproducibility data is shown in **Table 2**.

**Table 2.** Access Rubella IgG Assay Reproducibility (Between-Instrument Precision)

Sample	n	Mean (IU/mL)	Repeatability (Within-Run)		Between-Day/Run <sup>a</sup>		Between-Instrument		Between-Lot		Reproducibility <sup>b</sup>	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Sample 1	225	10.5	0.40	3.8	0.55	5.2	0.04	0.3	0.31	3.0	0.75	7.1
Sample 2	225	18.4	0.82	4.4	0.76	4.1	0.43	2.3	0.14	0.8	1.20	6.5
Sample 3	225	58.3	2.85	4.9	3.82	6.6	2.16	3.7	3.70	6.3	6.41	11.0
Sample 4	225	119.7	5.18	4.3	7.64	6.4	0.00	0.0	3.55	3.0	9.90	8.3
Sample 5	225	162.8	6.44	4.0	9.74	6.0	4.26	2.6	5.53	3.4	13.61	8.4
Sample 6	225	370.9	13.38	3.6	18.13	4.9	5.76	1.6	7.21	1.9	24.35	6.6

<sup>a</sup> Days and runs are confounded.

<sup>b</sup> Reproducibility includes within-run, between-run, between-day, and between-lot variance components.

- c) *Reproducibility (between-site precision)*: Refer to K954687.

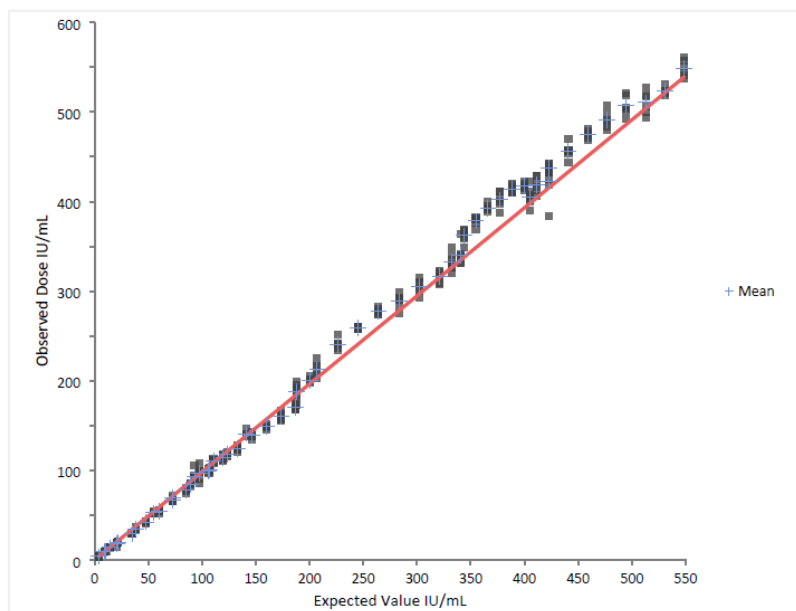
## 2. Linearity:

Linearity of the Access Rubella IgG on the DxI 9000 Access Immunoassay Analyzer was evaluated following CLSI Guideline EP06, 2nd Edition “Evaluation of Linearity of Quantitative Measurement Procedures”. A tiled approach was used to evaluate the linearity of six segments of the measuring range. Six sample panels were generated by diluting unique pairs of high and low Rubella IgG antibody positive serum samples in various ratios. Each panel consisted of 7 – 9 dilutions in addition to high and low concentration samples. The

table below indicates the number of dilutions and concentration ranges covered by each sample panel.

Panel	Concentration Range (IU/mL)	Number of Samples per Panel
1	3.87 – 140.97	9
2	9.42 – 110.56	11
3	92.92 – 200.53	9
4	188.02 – 340.47	9
5	332.23 – 422.55	9
6	405.11 – 548.77	9

This study was run on two DxI 9000 Access Immunoassay Analyzers, using one reagent lot and one calibrator lot. Low sample was run in replicates of eight, and all other samples were run in replicates of four or six. Two quality controls were run in replicates of two. The linearity of the Access Rubella IgG assay was considered acceptable if the data set was determined to be linear and if the deviation from linearity within or equal to  $\pm 10\%$  for samples with concentrations  $\geq 5.0$  IU/mL. This assay is linear across the analytical measuring interval of 5.0 to 500.0 IU/mL.



Regression equation:  $y = 0.9825x - 0.0819$

3. Analytical Specificity/Interference:

Refer to K954687.

4. Assay Reportable Range:

5.0 IU/mL – 500.0 IU/mL. See linearity above.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Refer to K954687. The Access Rubella IgG calibrators were standardized against the 2nd International Standard Preparation for Anti-Rubella Serum 2<sup>nd</sup> ISP.

6. Detection Limit:

The limit of blank (LoB), limit of detection (LoD) and Lower limit of quantitation (LLoQ) for the Access Rubella IgG assay on DxI 9000 Immunoassay Analyzer were established following CLSI guideline EP17-A2 (Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition). In order to obtain at least 60 replicates of each sample level, the LoB was established with 5 zero-analyte serum samples tested in replicates of 5 over 3 days; the LoD with 6 low-analyte serum samples tested in replicates of 9 over 5 days; and the LLoQ with 13 low-analyte serum samples tested in replicates of 9 over 5 days. Detection Limit for the Access Rubella IgG assay on the DxI 9000 Access Immunoassay Analyzer are:

LoB = 0.1 IU/mL.

LoD = 0.2 IU/mL.

LLoQ = 5.0 IU/mL.

7. Assay Cut-Off:

Refer to K954687.

8. Carry-Over:

Not applicable.

**B Comparison Studies:**

1. Comparison of Access Rubella IgG assay on the Access 2 Immunoassay System to the DxI 9000 Access Immunoassay Analyzer:

A method comparison study was conducted to compare the performance of the Access Rubella IgG assay on DxI 9000 Access Immunoassay Analyzer, to the Access Rubella IgG assay on the Access 2 Immunoassay System. A total of 162 native serum samples were tested on both instruments. PPA and NPA between the Rubella IgG assay when run on both systems are presented in **Table 3**.

**Table 3.** Performance Agreement of the Access Rubella IgG on the Access 2 Immunoassay System and the DxI 9000 Access Immunoassay Analyzer (n=162)

Access Rubella IgG		Access 2 Immunoassay System		
		Reactive	Equivocal	Non-reactive
DxI 9000 Access Immunoassay Analyzer	Reactive	77	0	0
	Equivocal	0	25	2
	Non-Reactive	0	2	56
	<b>Total</b>	77	27	58
	<b>PPA</b>	97.47% (77/79), 95% CI = 91.23% to 99.30%		
	<b>NPA</b>	96.55% (56/58), 95% CI = 88.27% to 99.05%		



2. Matrix Comparison:

Not applicable.

**C Clinical Studies:**

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

For clinical agreement study, refer to K954687.

**D Clinical Cut-Off:**

Not applicable.

**E Expected Values/Reference Range:**

Not applicable.

**VIII Proposed Labeling:**

The labeling supports the finding of substantial equivalence for this device.

**IX Conclusion:**

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