510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number
K203612

B Applicant
Immucor, Inc.

C Proprietary and Established Names
Capture-CMV

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LJO	Class II	21 CFR 866.3175 - Cytomegalovirus Serological Reagents	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:
Intent to market the Capture-CMV® assay for use with Galileo NEO® instrument intended for screening of patients for CMV infection.

B Measurand:
Adherence of the indicator red cells over the surface of the microtitration well, to indicate presence of IgM and IgG antibodies to CMV.

C Type of Test:
Qualitative; solid phase red cell adherence antibody system.

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below

B Indication(s) for Use:

Capture-CMV® is an in vitro qualitative solid phase red cell adherence test system for the detection of antibodies (IgG plus IgM) to cytomegalovirus (CMV) in human serum or plasma. Capture-CMV® is intended to be used in screening of patients for serological evidence of previous infection by CMV using manual and semi-automated methods, NEO Iris® and Galileo NEO®.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

The CMV assay is to be used with manual, semi-automated methods as well as with NEO Iris® and Galileo NEO® instruments.

IV Device/System Characteristics:

A Device Description:

Capture-CMV is a solid phase red cell adherence antibody detection system based on procedures of Plapp et al (1984;82:719).

The assay consists of Capture-CMV Microtitration Wells coated with glycine-extracted and purified CMV antigen obtained from cytomegalovirus strain AD 169 grown in human foreskin (HF) fibroblast cells.

Sold separately are the adjunct reagents to capture test wells and controls.

- Capture-CMV Indicator Red Cells: a suspension of human red blood cells coated with rabbit anti-human IgG plus goat anti-human IgM molecules;
- Capture LISS: a low ionic strength solution containing glycine, bromocresol purple dye and sodium azide
- Capture-CMV Positive Control Serum (weak): Human serum containing IgG antibodies to CMV viral proteins
- Capture-CMV Negative Control Serum: Human serum containing no antibodies to CMV

The CMV assay is to be used with manual, semi-automated methods as well as with NEO Iris® and Galileo NEO® instruments.

B Principle of Operation:

This procedure is a modification of the mixed agglutination tests for antigen and antibody detection of Coombs et al. (1956;2:84) and Hogman (1959;4:12).

The assay procedure is a two-step solid phase red cell adherence test carried out in microtitration wells coated with inactivated CMV virus. The CMV antigen utilized in this test is obtained from the cytomegalovirus strain AD 169 grown in human foreskin (HF) fibroblast cells. The inactivated virus is coated onto microtitration wells. The wells are dried and supplied to users along with necessary reagents and controls. Serum or plasma samples are added to the viral-coated wells and incubated for five minutes during which antibodies specific for CMV proteins bind to immobilized viral proteins. Unbound immunoglobulins are washed from the wells and replaced with a suspension of anti-IgG and anti-IgM-coated indicator red cells. Centrifugation brings the indicator red cells in contact with antibodies bound to the immobilized viral proteins. In the case of a positive test, the migration of the indicator cells to the bottom of the well is impeded as the anti-IgG and anti-IgM bridges are formed between the indicator red cells and the viralbound antibodies. As a consequence, the indicator red cells adhere over the surface of the

test well. In contrast, in the absence of viral antigen-antibody interactions (i.e. a negative test) the indicator red cells are not impeded during their migration, and pellet to the bottom of the well as a packed, well-defined cell button.
The image of cells adhered in the well is captured and analyzed by an instrument. The plate reader uses IDS CMOS camera to capture an image of the microplate from underneath. The software calculates a reaction value for each well based on a multi feature image analysis then assigns a result and interpretation to the wells based on predefined criteria associated with the calculated reaction value.

C Instrument Description Information:

1. Instrument Name:
   The NEO Iris® and Galileo NEO® instruments

2. Specimen Identification:
   The Gaileo NEO supports the use of the following barcode symbologies: Codabar; Code 128; ISBT 128 (Concatenated barcodes are not supported) and Code 39.

3. Specimen Sampling and Handling:
   A blood specimen is drawn using an acceptable phlebotomy technique. Serum or plasma (EDTA, CPD, CP2D, CPDA-1, ACD) may be used in this assay. Testing should be performed as soon as possible to minimize the chance that falsely positive or falsely negative reactions will occur due to improper storage or contamination of the specimen. Should delays in testing occur, serum or EDTA, CPD, and ACD anticoagulated whole blood specimens should be stored at 1-10°C for up to one week. Specimens collected in CP2D and CPDA-1 anticoagulants and stored as whole blood specimens at 1-10°C may be tested up to 42 days post-collection. Testing of CPDA-1 and ACD anticoagulated specimens stored at 18-25°C for five days is acceptable. Alternatively, serum or plasma can be separated from red cells and stored frozen at –20°C in a nondefrosting freezer refrigerator. Samples should not be repeatedly frozen and thawed.
   The Galileo NEO is programmed to move microplates, liquid reagent fluids, and blood sample fluids to different bays and processing areas for a given assay in the correct sequence. Such bays and areas include incubator bays, the microplate washing station, the centrifuge, and the reader.

4. Calibration:
   The instrument is calibrated at the site of manufacture using a reader verification plate (RVP). The plate is provided with the instrument to the end user, for calibration verification. Reader verification plate is stored in a protective case and should be replaced upon expiration that is three years from the calibration date which is the same as the release date provided on the Release Statement.

5. Quality Control:
   Capture-CMV Positive Control Serum
   Capture-CMV Negative Control Serum
   The reactivity of the Capture-CMV® assay is evaluated at each run by inclusion of the negative and weak positive controls. If, in any test run, the Positive Control Serum (Weak) does not produce positive results and/or the Negative Control Serum does not produce negative results, the NEO Iris®/Galileo NEO® will invalidate the test run and all the tests

performed in the run must be repeated. Continued failure of the control sera to perform properly may indicate that either one or more of the test reagents has deteriorated.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Capture-CMV®

B Predicate 510(k) Number(s):
K183571

C Comparison with Predicate(s):

Table 1.

Device & Predicate Device(s):	K203612	K183571
Device Trade Name	Capture-CMV®	Capture-CMV®
General Device Characteristic Similarities		
Intended Use/Indications for Use	Capture-CMV® is an in vitro qualitative solid phase red cell adherence test system for the detection of antibodies (IgG plus IgM) to cytomegalovirus (CMV) in human serum or plasma. Capture-CMV® is intended to be used in screening of patients for serological evidence of previous infection by CMV using manual and semi-automated methods, NEO Iris® and Galileo NEO®.	Capture-CMV® is an in vitro qualitative solid phase red cell adherence test system for the detection of antibodies (IgG plus IgM) to cytomegalovirus (CMV) in human serum or plasma. Capture-CMV is intended to be used in screening of blood and plasma donors or patients for serological evidence of previous infection by CMV.
Specimen/Sample	Serum or plasma	Serum or plasma
Test Principle	Same	Serum or plasma samples are added to the viral-coated wells. The samples are incubated for five minutes during which antibodies specific for CMV proteins bind to immobilized viral proteins. Unbound immunoglobulins are washed from the wells

		and replaced with a suspension of anti-IgG-plus anti-IgM-coated indicator red cells. Centrifugation brings the indicator red cells in contact with antibodies bound to the immobilized viral proteins. In the case of a positive test, the migration of the indicator red cells to the bottom of the well is impeded as the anti-IgG and anti- IgM bridges are formed between the indicator red cells and the viral-bound antibodies. As a consequence, the indicator red cells adhere over the surface of the microtitration well. In contrast, in the absence of viral antigen-antibody interactions (ie, a negative test) the indicator red cells are not impeded during their migration, and pellet to the bottom of the well as a packed, well-defined cell button
Assay contents Adjunct reagents purchased separately	Same	Capture-CMV Microtitration Wells Capture-CMV Indicator Red Cells Capture LISS Capture-CMV Positive Control Serum (weak) Capture-CMV Negative Control Serum
Shelf-life	Same	Test wells – 6 months Controls – 15 months Capture LISS – 12 months Indicator Red Cells – 60 days
Camera	Same	IDS CMOS camera module

Software	Same	Instrument software version 3.0.1.0
General Device Characteristic Differences		
Instrument	There is no difference between the two instruments except model name, the software setting that indicates the device name Galileo NEO® or NEO Iris® on the assay report and the exterior colors of the instruments.	

VI Standards/Guidance Documents Referenced:

Not applicable

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The Galileo NEO® instrument is identical to the NEO Iris® instrument, except branding and exterior colors. Thus, the CMV assay performance on Galileo NEO® is identical to the CMV assay performance on NEO Iris®. Consequently, the reproducibility data collected for the CMV assay on the NEO Iris® (K183571) were re-used in the current application and are summarized below.

Reproducibility of Capture-CMV® assay on NEO Iris® was determined at three test sites: two external sites and one internally at Immucor. A panel of ten coded samples was used: five CMV antibody positive and five CMV antibody negative. The samples were tested by two operators, in duplicate, two runs per day for five nonconsecutive days. A variance component analysis was performed based on the original raw scores. Reproducibility was assessed as concordance between the CMV assay result and the status of the sample. The summary of reproducibility results by site are presented in Table 2 below.

Table 2. Reproducibility of the CMV assay. Concordance by Site

Site	Total Tests	Expected Positive	Observed Positive	% Concordance (95% LCI)	Expected Negative	Observed Negative	% Concordance (95% LCI)
1	400	200	200	100.0% (98.5%)	200	200	100.0% (98.5%)
2	400	200	200	100.0% (98.5%)	200	200	100.0% (98.5%)
3	400	200	200	100.0% (98.5%)	200	199	99.5% (97.7%)
Total	1200	600	600	100.0% (98.5%)	600	599	99.8% (99.2%)

2. Linearity:
   Not applicable; this is a qualitative assay with the output: reactive/nonreactive

3. Analytical Specificity/Cross Reactivity:
   This study was performed to assess whether any cross reactivity occurs when testing samples that contain IgG antibodies to other viruses or conditions.

Table 3. Analytical Specificity		
Category of Specimen	Number	Capture-CMV Positive
EBV (VCA) Epstein-Barr Virus (Viral Capsid Antigen)	16	0
HSV – Herpes Simplex Virus	Type I – 10 Type II – 13 IgM* – 2	0
Hepatitis A	5	1
Parvovirus B19	4	0
ANA – Anti-Nuclear Antibodies	11	1
RF – Rheumatoid Factor	10	0
VZ – Varicella Zoster	8	0
Rubella	8	0
Toxoplasma gondii	4	0

*HSV Type not specified.

Assay limitations:
- Positive test results in symptomatic patients require careful interpretation since false-positive reactions or heterotypic IgM responses may occur with sera from patients with heterophile-positive mononucleosis or varicella zoster infection (see also the Product Insert)
- Care should be taken in interpreting test results of neonatal samples. A positive test usually indicates the presence of antibodies passively transferred from mother to fetus. A negative test may be helpful in excluding possible infection, but a diagnosis of active CMV infection may require viral culture.

4. Assay Reportable Range:
   Not applicable; this is a qualitative assay

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
   There were no changes to Capture-CMV® assay reagents and controls since it has been cleared under K183571.

6. Detection Limit:
   Not applicable; this is a qualitative assay with the output: reactive/nonreactive

7. Assay Cut-Off:
   The cutoff for the CMV assay is a well score 45.5. The well score is based on a multi-feature image analysis performed by the camera and the related software.

8. Accuracy (Instrument):
   The system verification activities for NEO Iris® included all testing performed related to the CMV assay as appropriate including assay performance for establishing equivalency. All documents generated to support the development, and operations of the system adhere to standard procedures. Testing was executed in accordance with the execution and test procedure instructions.
   Additional detailed information about the system verification can be found under the NEO Iris premarket notification BK180243. The results of the verification have been found acceptable to confirm safety and performance.

9. Carry-Over:
   There were no changes to Capture-CMV® assay reagents and controls since it has been cleared under K183571

B Comparison Studies:

1. Method Comparison with Predicate Device:
   No new clinical studies were performed as the NEO Iris® and the upgraded Galileo NEO® (software version 3.0.1) instruments are functionally identical. The data in the following tables were submitted for clearance of the NEO Iris® in K183571 and are included in the current submission to support clearance of the Capture-CMV® assay when used with the upgraded Galileo NEO® (software version 3.0.1). In these studies, the performance of the Capture-CMV® on NEO Iris® was compared with the performance of the assay on the original Galileo NEO® instrument (cleared in BK100033). For more information refer to K183571: Capture-CMV® (K183571 Decision Summary and 510(k) Summary).

   The following section provides a summary of the previous study and results. Method comparison studies were performed at four clinical sites, three external sites and internally at Immucor, Inc. for donor specimens and at two external sites and internally at Immucor, Inc. for patient specimens. Specimens were tested on NEO Iris® and Galileo NEO®. Test results were evaluated for agreement between analyzers. Specimens with discordant results were further tested with a commercially available particle agglutination assay for total antibody (IgG and IgM) to CMV.

   Specimen testing by sites:

   Table 4.

Sites	Patient Specimens		
	Total	Serum	Plasma
1	26	18	8
2	0	0	0
3	195	70	125
4	280	212	68

Table 5.

CMV Initial Results Patient Sample N=501		Galileo NEO®	
		Positive	Negative
NEO Iris®	Positive	272	5
	Negative	0	224
CMV Resolved Results		Galileo NEO® / FDA cleared assay *	
		Positive	Negative
NEO Iris®	Positive	272	5
	Negative	0	224
Sensitivity 100.0% (98.7%, 95% 2-sided LCI)			
Specificity 97.8% (95.0%, 95% 2-sided LCI)			

*Only discordant specimens were tested with FDA cleared IgG/IgM anti-CMV assay.

2. Matrix Comparison:
The clinical study performed in K183571 included data for EDTA (Ethylenediaminetetraacetic Acid), CP2D (Citrate Phosphate Double Dextrose), CPDA-1 (Citrate Phosphate Dextrose Adenosine), ACD (Anticoagulant Citrate Dextrose), AS-1 (Additive Solution 1), AS-3 (Additive Solution 3) and AS-5 (Additive Solution 5) as anticoagulants. The results demonstrated that these approved anticoagulants and additives did not adversely affect the data collection or sample results. Each anticoagulant is listed in the corresponding CMV package insert.

C Clinical Studies:

1. Clinical Sensitivity:
The Galileo NEO® (with software v. 3.0.1) instrument is identical to the NEO Iris® instrument that operates under the same software. Thus, CMV assay performance on Galileo NEO® (software version 3.0.1) is identical to its performance on NEO Iris®. The clinical sensitivity and specificity data collected for the CMV assay on the NEO Iris® (BK183571) were re-used in the current application and are summarized in section B.1. Method Comparison with Predicate Device, above.

2. Clinical Specificity:
Clinical specificity data are summarized in section B.1. Method Comparison with Predicate Device, above.

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

D Clinical Cut-Off:

The CMV assay cut-off is: Negative ≤ 45.5 <Positive

E Expected Values/Reference Range:

Not applicable; this is a qualitative assay

F Other Supportive Instrument Performance Characteristics Data:
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.