510(k) Summary

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510(k) Owner

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Contact Information

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Device Name

Trade/Device Name:	Capture-CMV®
Common Name:	Test, Donor, CMV
Classification Name:	Test, Donor, CMV
Unique Device Identifier (UDI):	10888234002154

Device Class

Regulatory Class:	II
Product Code:	MZE
Regulation Number:	21 C.F.R.§866.3175

Predicate Device Information

Trade/Device Name:	Capture-CMV®
Clearance:	BK180247 (cleared November 20, 2018)

Purpose of the Submission

Demonstrate performance of the Capture-CMV® assay on the upgraded Galileo NEO® (Software version 3.0.1) instrument. This is an upgrade of the Galileo NEO® (BK100033) to match the NEO Iris® instrument that was cleared via BK180247, BK200474 and BK200502.

With these changes the Galileo NEO® and NEO Iris® instruments are functionally identical: the only differences are model name, the exterior colors of the instruments, and whether the software indicates the device name as NEO Iris® or Galileo NEO®. Thus, no new studies were performed to evaluate the performance of Capture-CMV®. Instead, previous data supporting the original clearance of the Capture-CMV® assay on the NEO Iris® is presented.

Intended 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 blood and plasma donors for serological evidence of previous infection by CMV using the NEO Iris® and Galileo NEO®. This assay is not intended for diagnostic use.

Device Description

Capture-CMV® is a Solid Phase System for the Detection of IgG and IgM Antibodies to Cytomegalovirus (CMV).

Cytomegalovirus (CMV) is a common human viral pathogen which belongs to the family of herpes viruses. The presence of CMV antibodies in an individual indicates prior infection by the virus. The possibility exists that viral reactivation can occur in such individuals. CMV infection is usually asymptomatic and can persist as a latent or chronic infection.

Viral transmission may occur through transfusion of blood or transplantation of organs from seropositive donors.

Immunocompromised patients, such as premature neonates, organ transplant patients, and oncology patients, are at greater risk of developing more severe manifestations of CMV infections which can be a major direct or indirect cause of mortality in such patients.

Congenitally infected newborns are especially prone to developing severe cytomegalic inclusion disease (CID). The severe form of CID may be fatal or may cause permanent neurological sequelae, such as mental retardation, deafness, microcephaly, and motor dysfunction. A CMV mononucleosis-type syndrome can result from the transfusion of CMV-infected blood products or the transplantation of CMV-infected donor organs in a seronegative immunocompromised patient. Low birth weight neonates are also at high risk to CMV mononucleosis through transfusion of CMV-infected blood products.

One method of preventing or reducing CMV infection in seronegative immunocompromised patients is to select CMV seronegative blood donors or organ donors that have been tested by serological screening test for antibodies to CMV. Capture-CMV® is a solid phase red cell adherence antibody detection system based on procedures of Plapp et al[1]. This procedure is a modification of the mixed agglutination tests for antigen and antibody detection of Coombs et al.[2] and Hogman[3] employing anti-IgG and IgG-coated red cells as the indicator system. Capture assays for the detection of antibodies to red cells or platelets use anti-IgG-coated red cells as the indicator. Capture-CMV® uses anti-IgG plus anti-IgM-coated indicator red cells.

The CMV assay is to be used with NEO Iris® and the Galileo NEO® instruments

The NEO Iris®/Galileo NEO® is a microprocessor-controlled instrument that fully automates test processing, result interpretation and data management functions for the associated assays. The instrument is designed to automate, in addition to the CMV assay, standard immunohematology assays using a microplate-based platform.

The originally cleared Galileo NEO® (BK100033) was updated with the following modifications in the current submission:

- The Digi CCD camera module was replaced with an IDS CMOS camera module
- Galileo NEO® software was replaced with NEO Iris® Install Set 3.0.1.0 U software and configuration files
- Galileo NEO® versions of the files OiBxEngl.dll and GalileoLogo.bmp were installed to preserve Galileo NEO® branding in the User Interface and on Reports

For detailed technological characteristics of the upgraded Galileo NEO® and the NEO Iris® instrument refer to the following clearance documents: BK100033, BK180243, BK180247, BK200474 and BK200502.

Substantial Equivalence and Comparison to the Predicate Device

Technological Characteristics	PREDICATE DEVICE: BK180247 (Capture-CMV® cleared for use on NEO Iris® November 20, 2018)	PROPOSED DEVICE: Capture-CMV (for use on upgraded Galileo NEO®)	Comparison
Intended Use	The Immucor 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 for serological evidence of previous infection by CMV using the NEO Iris®. This assay is not intended for diagnostic 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 blood and plasma donors for serological evidence of previous infection by CMV using the NEO Iris® and Galileo NEO®. This assay is not intended for diagnostic use.	Equivalent – Indications for use (add Galileo NEO® with software version 3.0.1 for donor screening)
Test Principle	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 (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.	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 (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.	Identical
Test Wells	CMV antigen from cytomegalovirus strain AS 169 grown in human foreskin fibroblast cells is inactivated and coated onto microtitration wells and dried.	CMV antigen from cytomegalovirus strain AS 169 grown in human foreskin fibroblast cells is inactivated and coated onto microtitration wells and dried.	Identical
Capture-CMV® Positive Control Serum (Weak)	Human serum containing IgG antibodies to CMV viral proteins. Capture-CMV® Positive Control Serum (weak) is manufactured to represent the reactivity obtained by weak CMV antibody positive donors. Weak CMV antibody positive donors have a titration endpoint of 1:2 or less. Sodium azide (0.1%) has been added as a preservative.	Human serum containing IgG antibodies to CMV viral proteins. Capture-CMV® Positive Control Serum (weak) is manufactured to represent the reactivity obtained by weak CMV antibody positive donors. Weak CMV antibody positive donors have a titration endpoint of 1:2 or less. Sodium azide (0.1%) has been added as a preservative.	Identical
Capture-CMV® Negative Control Serum	Human serum containing no antibodies to CMV. Sodium azide (0.1%) has been added as a preservative.	Human serum containing no antibodies to CMV. Sodium azide (0.1%) has been added as a preservative.	Identical

Technological Characteristics	PREDICATE DEVICE: BK180247 (Capture-CMV® cleared for use on NEO Iris® November 20, 2018)	PROPOSED DEVICE: Capture-CMV (for use on upgraded Galileo NEO®)	Comparison
Capture-CMV® Indicator Red Cells	A suspension of human red blood cells coated with rabbit anti-human IgG plus goat anti-human IgM molecules. The red blood cells are suspended in a buffered solution to which chloramphenicol (0.25 mg/mL), neomycin sulfate (0.1 mg/mL) and gentamycin sulfate (0.05 mg/mL) have been added as preservatives.	A suspension of human red blood cells coated with rabbit anti-human IgG plus goat anti-human IgM molecules. The red blood cells are suspended in a buffered solution to which chloramphenicol (0.25 mg/mL), neomycin sulfate (0.1 mg/mL) and gentamycin sulfate (0.05 mg/mL) have been added as preservatives.	Identical
Capture®-LISS	A low ionic strength solution containing glycine, bromocresol purple dye and the preservative sodium azide (0.1%).	A low ionic strength solution containing glycine, bromocresol purple dye and the preservative sodium azide (0.1%).	Identical
Shelf-life	Test wells – 6 months Controls – 15 months Capture-LISS – 12 months Indicator Red Cells – 60 days	Test wells – 6 months Controls – 15 months Capture-LISS – 12 months Indicator Red Cells – 60 days	Identical
Specimen/ Sample	Serum or plasma	Serum or plasma	Identical
Test Methods	• Manual (BK950029) • Galileo® (BK050050) • Galileo NEO® (BK100033[1] /BK170067[2]) • NEO Iris® (BK180247[3]) 1) Capture-CMV® cleared for use on the Galileo NEO®. 2) Capture-CMV® cleared for use on the Galileo NEO® (Special 510(k) submission filed to update analyzer modifications only). 3) Capture-CMV® cleared for use on NEO Iris®	• Manual • Galileo® • Galileo NEO® • NEO Iris® Galileo NEO® with software version 3.0.1	Equivalent – Indications for use (add Galileo NEO® with software version 3.0.1 for donor screening)

Performance Data and Testing – Non-Clinical

As noted in the Device Description section above, this submission describes an upgrade of the Galileo NEO® instrument, making it functionally identical to the NEO Iris®. As such, no new studies were performed. Instead, previous data supporting the original clearance of the Capture-CMV® assay on the NEO Iris® (BK180247) are presented to demonstrate performance of the upgraded Galileo NEO® system.

The system verification activities for NEO Iris® were performed as defined in Verification Plan 14-012-VRPLN at Immucor's facility in Norcross, GA. The verification activities 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.

Additional and detailed information about the upgraded Galileo NEO® (software version 3.0.1) 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 (which can be found under the Capture-CMV® premarket notification BK180247).

Performance Data and Testing – Clinical

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 BK180247 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® with NEO Iris® was compared with the performance of the assay on the original Galileo NEO® instrument (cleared in BK100033). For more information refer to BK180247: Capture-CMV® (BK180247 Letter and BK180247 Summary)

In BK180247, the method comparison studies were performed at four clinical sites, three external sites and one internally at Immucor, Inc. Donor 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 FDA cleared particle agglutination assay for total antibody (IgG+IgM) to CMV.

Specimen testing by sites

Sites	Total Donor Specimens Tested	Donor Specimens	
		Serum	Plasma
1	474	57	417
2	289	59	230
3	103	20	83
Immucor	382	70	312

CMV Initial Results Donor Samples N=1248		Galileo NEO®	
		Positive	Negative
NEO Iris®	Positive	612	8
	Negative	27	601
CMV Resolved Results		Galileo NEO® / FDA cleared assay*	
		Positive	Negative
NEO Iris®	Positive	612	8
	Negative	1	627
Sensitivity 99.8% (99.1%, 95% 2-sided LCI)			
Specificity 98.7% (97.5%, 95% 2-sided LCI)			

LCI – Lower Confidence Interval

CMV Initial Results Donor Serum Samples N=206		Galileo NEO®	
		Positive	Negative
NEO Iris®	Positive	103	1
	Negative	5	97
CMV Resolved Results		Galileo NEO® / FDA cleared assay*	
		Positive	Negative
NEO Iris®	Positive	103	1
	Negative	0	102
Sensitivity 100.0% (96.5%, 95% 2-sided LCI)			
Specificity 99.0% (94.7%, 95% 2-sided LCI)			

CMV Initial Results Donor Plasma Samples N=1042		Galileo NEO®	
		Positive	Negative
NEO Iris®	Positive	509	7
	Negative	22	504
CMV Resolved Results		Galileo NEO® / FDA cleared assay*	
		Positive	Negative
NEO Iris®	Positive	509	7
	Negative	1	525
Sensitivity 99.8% (98.9%, 95% 2-sided LCI)			
Specificity 98.7% (97.3%, 95% 2-sided LCI)			

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

Results are for North America Market assays.

Reproducibility

The reproducibility of Capture-CMV® assay on the NEO Iris®† was determined using a panel of ten (10) coded samples, five (5) CMV antibody positive and five (5) CMV antibody negative, at three (3) test sites, two external sites and internally at Immucor. The samples were tested by two operators, in duplicate on two (2) runs per day for five (5) nonconsecutive days. The summary of reproducibility results by site are presented in the following table:

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% (98.2%)	200	200	100.0% (98.2%)
2	400	200	200	100.0% (98.2%)	200	200	100.0% (98.2%)
3	400	200	200	100.0% (98.2%)	200	199	99.5% (97.2%)
Total	1200	600	600	100.0% (99.6%)	600	599	99.8% (99.1%)

† Assay performance on Galileo NEO® (Software version 3.0.1 or higher) is identical to performance on NEO Iris®.

Conclusion

The non-clinical and clinical study data demonstrate that the Capture-CMV® assay used with Galileo NEO® instrument is as safe and effective as the predicate device.

Bibliography

1. Plapp FV, Sinor LT, Rachel JM et al. A solid phase antibody screen. Am J Clin Pathol 1984;82:719.
2. Coombs RRA, Marks J, Bedford D. Specific mixed agglutination: Mixed erythrocyte-platelet anti-globulin reactions for the detection of platelet antibodies. Br J Haematol 1956;2:84.
3. Hogman C. The principle of mixed agglutination applied to tissue culture systems. Vox Sang 1959;4:12.