Section 5 510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

A. 510(k) Number: BK200476

B. Purpose for Submission:

New device; the purpose of this submission is to add the Beckman Coulter PK7400 Automated Microplate System (blood bank analyzer) to the PK CMV-PA System, which was previously cleared using the Beckman Coulter PK7300 Automated Microplate System (BK070030). The PK CMV-PA System has not been modified for use with the PK7400 and are the same formulation as was previously cleared. The only modification proposed for this submission is the addition of the PK7400 Automated Microplate System (and related performance and operational instructions) to the intended use and package inserts for the referenced devices.

C. Measurand:

IgG and IgM antibodies to cytomegalovirus (CMV) in human plasma and serum

D. Type of Test:

Qualitative, passive particle agglutination assay on the Beckman Coulter PK7300 and/or PK7400 Automated Microplate Systems

E. Applicant:

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F. Proprietary/Established and Common Names:

1. Proprietary/Established Names:
   PK CMV-PA System

2. Common Name:
   CMV

G. Regulatory Information:

1. Regulation section:
   21 CFR § 866.3175, CMV Serological Reagents

2. Classification:
   Class II

3. Product code:
   MZE

4. Panel:
   Immunology

H. Intended Use:

1. Intended use(s):
   The PK CMV-PA System is a passive particle agglutination assay intended for the qualitative detection of IgG and IgM antibodies to cytomegalovirus (CMV) in human EDTA plasma and serum from blood donors using the Beckman Coulter PK7300 and/or PK7400 Automated Microplate Systems. This test is not intended for diagnostic use.

2. Indication(s) for use:
   Same as intended use above.

3. Special conditions for use statement(s):
   Prescription use only

4. Special instrument requirements:
   Beckman Coulter PK7300 and/or PK7400 Automated Microplate Systems

I. Device Description:

Cytomegalovirus (CMV) is a double-stranded DNA virus with physicochemical characteristics common to members of the herpesvirus family. Serologic surveys have shown that CMV infection is worldwide in distribution, with antibody prevalence in adults in the range of 20–82%. The majority of CMV infections are subclinical or associated with nonspecific illness. The virus may remain in a latent state indefinitely following initial infection, or it may emerge from time to time to cause an active infection. Pregnant women can transmit the CMV virus to the fetus, resulting in congenital liver, spleen, and/or CNS disease in the unborn child. The congenital effects of mother-to fetus CMV transmission may be more severe in those cases where the mother has acquired the primary infection during early pregnancy than in maternal cases of reactivated disease. CMV infection often induces life-threatening conditions such as pneumonia, fever, and hepatitis among immunosuppressed patients such as organ transplant recipients and in patients harboring human immunodeficiency virus (HIV).

The transfusion or transplant of CMV seropositive blood or organs may cause a variety of clinical abnormalities in immunocompromised recipients. Since CMV infections are frequently transmitted through organ transplants and blood transfusions, the screening of blood donors for CMV antibodies is an important step toward reducing CMV infection in immunocompromised transfusion and transplant recipients. A variety of methods have been developed to detect antibodies to CMV including indirect hemagglutination assay (IHA), indirect fluorescent assay (IFA), anticomplement immunofluorescence (ACIF), enzyme immunoassay (EIA), or passive latex agglutination (PLA).

In 1951 Boyden succeeded in attaching a variety of protein antigens to the surfaces of tannic acid-treated sheep erythrocytes and demonstrated hemagglutination in the presence of the corresponding antibodies. Variations of these methods are still widely used today despite problems associated with biological carriers. To address these problems, artificial carriers have been developed as substitutes for erythrocytes and are now being used in immune agglutination assays for the detection of antibodies to various infectious diseases.

Automation has enhanced the value of the indirect particle agglutination test by significantly reducing the amount of time and labor needed to perform the assay. The PK CMV-PA System and PK CMV-PA System Control Set were developed to provide an indirect particle agglutination CMV assay using uniform reagents which are stable, easy to handle, and suitable for use on the Beckman Coulter PK7300, and PK7400 Automated Microplate Systems.

PK CMV-PA System

The PK CMV-PA System is available in a kit sufficient to perform 2300 tests and contains Reconstituting Solution, Sensitized Particles and Sample Diluent.

Kit	Contents	Volume
PK CMV-PA System	SENSITIZED PARTICLES: Gelatin particles colored with blue dye, sensitized with cytomegalovirus antigens and then lyophilized. Each vial must be reconstituted with 6.0 mL RECONSTITUTING SOLUTION. Reconstituted particles contain 0.15% sodium azide.	10 vials
	RECONSTITUTING SOLUTION: Phosphate buffered saline containing 0.10% sodium azide. Reconstituted particles contain 0.15% sodium azide.	1 bottle, 70 mL
	SAMPLE DILUENT: Proprietary solution containing phosphate buffered saline, normal rabbit serum and 0.10% sodium azide.	3 bottles, 300 mL

Other Materials/Equipment Required (not Provided):

Beckman Coulter Microplates with a 5µm well terraces
Pipetting device capable to delivering 6.0 mL
Beckman Coulter PK7300 and/or PK7400
PK CMV-PA System Control Set

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Olympus PK CMV-PA Test System and Controls (Originally manufactured for and distributed by Olympus, the product line was included in the acquisition of the Olympus Diagnostic Systems group by Beckman Coulter, Inc. in August 2009. Subsequently, regulatory registrations were updated accordingly, and Beckman Coulter branding was

phased in for the associated products) for the Olympus PK7300 Automated Microplate System.

2. Predicate 510(k) number(s):
BK070030

3. Comparison with predicate:

Similarities		
	PK CMV-PA System (Proposed Device)	**Olympus PK CMV-PA Test System and Controls for the Olympus PK7300 Automated Blood Bank Analyzer (Predicate Device) BK070030**
Device Type	*In vitro* diagnostic	*In vitro* diagnostic
Classification	Class II	Class II
CFR section	21 CFR 866.3175	21 CFR 866.3175
Product Code	MZE	MZE
Intended Use	The PK CMV-PA System is a passive particle agglutination assay intended for the qualitative detection of IgG and IgM antibodies to cytomegalovirus (CMV) in human EDTA plasma and serum from blood donors using the Beckman Coulter PK7300 and/or PK7400 Automated Microplate Systems. This test is not intended for diagnostic use.	The OLYMPUS PK CMV-PA SYSTEM is a passive particle agglutination assay intended for the qualitative detection of IgG and IgM antibodies to cytomegalovirus (CMV) in human plasma and serum from blood donors using the OLYMPUS PK7200 and/or PK7300 Automated Microplate Systems. A positive result provides evidence of past or current infection with CMV. This test is not intended for diagnostic use.
Type of Specimen	Human EDTA plasma and Serum	Human EDTA Plasma and Serum
Analyte	IgG and IgM to Cytomegalovirus (CMV)	IgG and IgM to Cytomegalovirus (CMV)
Reaction Technology	Particle Agglutination	Particle Agglutination
Reaction Vessel	Beckman Coulter Terraced Microplates	Beckman Coulter Terraced Microplates
Instrument Process	Scanning photometer system of each plate well with CCD camera-based reaction image analysis & interpretation. The CCD converts light to electrical signals.	Scanning photometer system of each plate well with CCD camera-based reaction image analysis & interpretation. The CCD converts light to electrical signals.
Image Analysis Measurements	SPC, P/C, LIA	SPC, P/C, LIA
Assay-specific software	None	None

Similarities		
	PK CMV-PA System (Proposed Device)	**Olympus PK CMV-PA Test System and Controls for the Olympus PK7300 Automated Blood Bank Analyzer (Predicate Device) BK070030**
Throughput	300 samples per hour	300 samples per hour
Reaction Time (Incubation)	60 minutes	60 minutes
User Traceability	• Bar Coded Samples • Bar Coded Reagents & Diluents • Bar Coded Microplates	• Bar Coded Samples • Bar Coded Reagents & Diluents • Bar Coded Microplates
Reaction and Test Interpretation	Image analysis & reaction interpretation are based on 6 parameters. Decision logic utilizes 3 of these parameters (in bold font below) to interpret each reaction in each microplate well. Values for each of these three measurements are assessed against pre-programmed thresholds to interpret the reaction in each well as "+", "-", or "?". The reaction interpretations for each well are then compared to test logic tables to obtain the interpretation (result) for each test. The parameters are: • P: light transmittance in the test well periphery • C: light transmittance in the test well center region • BG: light transmittance outside the test well (background) • SPC: Indicates the sharpness at the edge of the cell button at the border of the P and C regions. • P/C: ratio of transmitted light between P and C regions • LIA: size and density of the cell button (low intensity area)	Image analysis & reaction interpretation are based on 6 parameters. Decision logic utilizes 3 of these parameters (in bold font below) to interpret each reaction in each microplate well. Values for each of these three measurements are assessed against pre-programmed thresholds to interpret the reaction in each well as "+", "-", or "?". The reaction interpretations for each well are then compared to test logic tables to obtain the interpretation (result) for each test. The parameters are: • P: light transmittance in the test well periphery • C: light transmittance in the test well center region • BG: light transmittance outside the test well (background) • SPC: Indicates the sharpness at the edge of the cell button at the border of the P and C regions. • P/C: ratio of transmitted light between P and C regions • LIA: size and density of the cell button (low intensity area)

Differences		
	PK CMV-PA System (Proposed Device)	**Olympus PK CMV-PA Test System and Controls for the Olympus PK7300 Automated Blood Bank Analyzer (Predicate Device) BK070030**
Instrument System	Closed System (only accepts the specified Beckman Coulter reagents)	Open System
Operating System	Microsoft Windows – 10 IoT	Currently: Support Microsoft Windows Embedded Standard 2009
Reagent Reconstitution Time	Minimum of 180 min	Minimum of 30 min
Incubation Temperature Setting (sample with sensitized particles)	30°C ± 2°C	28°C ± 2°C
Image Sensor (charge coupled device camera)	Digital CCD color camera for electronic image analysis of the PK microplates	CCD color camera for electronic image analysis of the PK microplates
Light source	LED light	Fluorescent lamp
Image Processing PCB	Calculates the image analysis pixels from the digital CCD camera	Calculates the image analysis pixels from the CCD color camera
Sample dispensing for plasma & serum	Dispense volume: 1-5 cups: 10-150 µL/cup sum total max 200 µL 2 cups: 120-150 µL/cup sum total max 270 µL	Dispense volume: 4 cups: 10-150 µL/cup sum total max 200 µL 2 cups: 120-150 µL/cup sum total max 270 µL
Sample dispensing order to the dilution cup	A›X›B›C›D (order of dispensing changed to reduce likelihood of contamination of diluted plasma with residual RBC from the sample probe)	D›C›B›X›A

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

- N/A

L. Test Principle:

The PK CMV-PA System uses gelatin particles coated with cytomegalovirus antigens to detect IgG and IgM antibodies to CMV in human serum and plasma. The test sample or control material is diluted with Sample Diluent and then mixed with the sensitized particles in a terraced microplate well. During the incubation, the particles settle in the terraced microplate well. Antibody to CMV will bind to the antigen-sensitized particles during this incubation. Particles with bound antibody will form agglutination, which are visible as a homogeneous blue layer of gelatin particles. When

antibodies to CMV are not present, sensitization and subsequent agglutination does not occur. Particles without bound antibody fall freely to the center of the well and visually appear as a compact dense blue button surrounded by a clear zone.

The PK7300 and/or PK7400 instrument will read the settling patterns of particles in each well based on the threshold settings chosen for the reagent. The PK7300 and/or PK7400 determines the presence or absence of antibodies to CMV using a CCD (charged coupled device) camera, which captures the well image allowing differentiation of agglutinated and unagglutinated patterns.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

NOTE: Studies denoted with an * were not retested on the PK7400 as the reagents were not changed.

a. Analytical Specificity:

*1. Interfering Substances and Microbial Contamination**

Reactive and Non-reactive PK CMV-PA System Controls were spiked with different concentrations of interfering substances and a pool of microbial suspension. The spiked samples were tested against three (3) lots of PK CMV-PA System reagents on the PK7300. Samples were tested on Day (b) (4) and Day (b) (4). Results are summarized below:

(b) (4) Interference:
- Elevated levels of (b) (4) had no effect on the non-reactive nor reactive control samples up to (b) (4).

(b) (4) Interference:
- Elevated levels of (b) (4) substance had no effect on reactive samples up to concentrations of (b) (4).
- For non-reactive samples:
  - Lot # 1 yielded correct results for (b) (4) non-reactive samples up to (b) (4) tested at day (b) (4) and on day (b) (4).
  - Lot #2 yielded correct results for (b) (4) non-reactive samples at (b) (4) on day (b) (4). Day (b) (4), (b) (4) non-reactive samples yielded correct results at (b) (4). The sample that did not yield correct results was titered down to a (b) (4) concentration of (b) (4) and yielded correct results at (b) (4).
  - Lot # 3 yielded correct results for (b) (4) non-reactive samples up to (b) (4) tested at day (b) (4) and on day (b) (4).

(b) (4) Interference:
- All reactive and non-reactive samples yielded correct results up to (b) (4) when tested at Day (b) (4) and Day (b) (4).

(b) (4) Interference:
- All reactive and non-reactive samples yielded correct results up to (b) (4) when tested at Day (b) (4) and Day (b) (4).

(b) (4) Interference:
- All reactive and non-reactive samples yielded correct results when tested at Day (b) (4) and Day (b) (4).

2. Stability:*

a. On-board sample stability:

One thousand one hundred fifty-four (1154) blood donor samples were used in this study to show that CMV testing on the PK7300 using the PK CMV-PA System reagent performs an accurate analysis of samples up to 5 days post collection. The lower confidence bound for the rate of agreement remained about 94% (all were greater than 98.0%) at 4 days and 6 days post collection. There was no loss of sensitivity and minimal loss of specificity.
Samples can be safely stored on the PK7300 using the PK CMV-PA System up to five days post collection.

b. Sample Freeze-thaw:

Twenty-seven (27) samples (b) (4)) were evaluated for correlation with the PK7200 (reference method). The samples were frozen and retested for (b) (4) cycles.
All samples resulted as expected as (b) (4) freeze thaw cycles.
As a result, Freezing and thawing does not impact CMV results.
Additionally, ANA, RF and Lyme positive samples did not interfere with CMV test results.

b. *Reproducibility:*

The reproducibility of the PK CMV-PA System on the PK7400 was evaluated at three sites using three lots (one lot per site) by testing 12 plasma and serum samples. Out of the 12 samples, 6 were known reactive and 6 known non-reactive samples. All samples were tested in duplicate, in two different runs per testing day (at least 2 hours apart), over a minimum of 5 nonconsecutive days. Results are summarized in Tables 1 and 2.

TABLE 1. REPRODUCIBILITY OF THE PK CMV-PA SYSTEM ON THE PK7400 FOR ALL LOTS/SITES

Sample ID	Expected Result	# Correct Results		% Correct Results
		Run 1	Run 2	
2400016401	Pos	30/30	30/30	100%
2400016402	Pos	30/30	30/30	100%
2600016403	Pos	30/30	30/30	100%
2600016404	Pos	30/30	30/30	100%
9245209	Neg	30/30	30/30	100%
2400016406	Pos	30/30	30/30	100%
103459900	Neg	30/30	30/30	100%
1034550100	Neg	30/30	30/30	100%
1034550400	Neg	30/30	30/30	100%
1034550500	Neg	30/30	30/30	100%
1034551000	Neg	30/30	30/30	100%
1034549600	Pos	30/30	30/30	100%

TABLE 2. REPEATABILITY OF THE PK CMV-PA SYSTEM ON THE PK7400 FOR ALL LOTS/SITES

Sample ID #	Expected Result	# Correct Results		% Correct Results
		Channel 11	Channel 12	
2400016401	Pos	15/15	15/15	100%
2400016402	Pos	15/15	15/15	100%
2600016403	Pos	15/15	15/15	100%
2600016404	Pos	15/15	15/15	100%
9245209	Neg	15/15	15/15	100%
2400016406	Pos	15/15	15/15	100%
103459900	Neg	15/15	15/15	100%
1034550100	Neg	15/15	15/15	100%
1034550400	Neg	15/15	15/15	100%
1034550500	Neg	15/15	15/15	100%
1034551000	Neg	15/15	15/15	100%
1034549600	Pos	15/15	15/15	100%

2. Comparison studies:

a. Method comparison with predicate device:

The performance of the PK CMV-PA System was evaluated on the PK7400 by comparing to the PK7300 reference results. Testing was performed at three geographically distinct blood centers. A total of 3372 serum samples and 3689 plasma (EDTA) samples were tested. Results are summarized in Tables 3 and 4.

TABLE 3. REFERENCE METHOD (PK7300) COMPARISON TO PK7400 - PLASMA ALL LOTS/SITES:

All Sites/Lots	Trial PK7400			Statistical Summary				
Reference PK7300	R	NR	Total		Agreement	Total	Rate of Agreement (%)	Lower 95% confidence bound
R	1690	2	1692	PPA	1690	1692	99.88%	99.57%
NR	6	1991	1997	NPA	1991	1997	99.70%	99.35%
Total	1696	1993	3689	OPA	3681	3689	99.78%	99.57%

TABLE 4. REFERENCE METHOD (PK7300) COMPARISON TO PK7400 - SERUM: ALL LOTS/SITES

All Sites/Lots	Trial PK7400			Statistical Summary				
Reference PK7300	R	NR	Total		Agreement	Total	Rate of Agreement (%)	Lower 95% confidence bound
R	1485	0	1485	PPA	1485	1485	100.00%	99.75%
NR	2	1885	1887	NPA	1885	1887	99.89%	99.62%
Total	1487	1885	3372	OPA	3370	3372	99.94%	99.79%

3. Clinical studies:

a. Sensitivity and Specificity

Sensitivity and Specificity for the PK CMV-PA System when tested on the PK7400 was determined by comparing the 3372 serum samples and the 3689 plasma samples from method comparison testing to the "true" result obtained on the PK7300. Discordant samples were tested by two other methods (DiaSorin LIAISON assay and Immucor

Capture-CMV). Best two out of three results was considered the "true" result after additional testing. Results are summarized in Tables 5 through 8.

TABLE 5. SENSITIVITY OF THE PK CMV-PA SYSTEM ON THE PK7300

Sample Type	True Result Positive	Incorrect Negative Result	Sensitivity	Lower 95% confidence bound
EDTA Plasma	1690	0	1690/1690 100.0%	99.78%
Serum	1485	1	1485/1486 99.93%	99.63%

TABLE 6. SPECIFICITY OF THE PK CMV-PA SYSTEM ON THE PK7300

Sample Type	True Result Negative	Incorrect Positive Result	Specificity	Lower 95% confidence bound
EDTA Plasma	1997	2	1997/1999 99.90%	99.64%
Serum	1886	0	1886/1886 100.0%	99.80%

TABLE 7. SENSITIVITY OF THE PK CMV-PA SYSTEM ON THE PK7400

Sample Type	True Result Positive	Incorrect Negative Result	Sensitivity	Lower 95% confidence bound
EDTA Plasma	1690	0	1690/1690 100.0%	99.78%
Serum	1486	0	1486/1486 100.0%	99.75%

TABLE 8. SPECIFICITY OF THE PK CMV-PA SYSTEM ON THE PK7400

Sample Type	True Result Negative	Incorrect Positive Result	Specificity	Lower 95% confidence bound
EDTA Plasma	1993	6	1993/1999 99.70%	99.35%
Serum	1885	1	1885/1886 99.95%	99.70%

N. Proposed Labeling:

The labeling satisfies the requirements of 21 CFR 809.10

O. Conclusion:

The results of these analytical (nonclinical) and clinical studies demonstrate that the PK CMV-PA System on the Beckman Coulter PK7400 Automated Microplate System is as safe, as effective, and performs as well as the performance of PK CMV-PA System on the Beckman Coulter PK7300 Automated Microplate System.