SECTION 5

510(k) SUMMARY

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510(k) Summary

5.1 SUBMITTER

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5.2 DEVICE

Name of device:	PK7400 TP HA Reagent PK7400 TP HA Controls
Classification name:	Treponema pallidum treponemal test reagents
Regulation:	21 CFR 866.3830
Regulatory class:	Class II
Product code:	MYR (Reagent); GMR (Controls)

5.3 PREDICATE DEVICE

Name of device:	Beckman Coulter PK TP System Beckman Coulter PK TP System Control Set
510(k):	BK060062

This device has not been subject to a design related recall.

5.4 DEVICE DESCRIPTION

PK7400 TP HA REAGENT test is based on the principle of agglutination and pattern recognition. The REAGENT uses preserved avian erythrocytes sensitized with extracted antigens of *T. pallidum* (Nichols strain). The EDTA plasma, CPDA plasma or serum test sample is diluted in a SAMPLE DILUENT, which uses absorbents to minimize nonspecific reactions. The REAGENT is added to the diluted test mixture and reactants are allowed to settle in a terraced microplate. Hemagglutination occurs in the presence of *Treponema pallidum* antibodies in specimens. Visually, a reactive test is a homogenous layer of cells. A nonreactive test would result in a compact dense button surrounded by a clear zone. The PK7400 reads the settling patterns of the erythrocytes in each well based on the threshold settings chosen for each reagent. The Beckman Coulter PK7400 captures the well images using a CCD (charged couple device) camera and subsequently uses the threshold settings in its algorithm to differentiate agglutinated and unagglutinated patterns.

5.5 INDICATIONS FOR USE

PK7400 TP HA REAGENT is intended for the qualitative screening of blood and plasma donors for the detection of *Treponema pallidum* IgG and IgM antibodies to syphilis in human serum, EDTA plasma or CPDA plasma using the Beckman Coulter PK7400 Automated Microplate System.

This assay is not intended for diagnostic use.

PK7400 TP HA CONTROLS are intended for use with the PK7400 TP HA REAGENT for the qualitative screening of blood and plasma donors for the detection of *Treponema pallidum* IgG and IgM antibodies to syphilis in human serum, EDTA plasma or CPDA plasma using the Beckman Coulter PK7400 Automated Microplate System.

5.6 COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

Characteristic	PREDICATE	PK7400 TP HA Reagent PROPOSED
Reagent System	PK TP System BK060062	PK7400 TP HA Reagent BK180301
Device Class, Regulation Code	Class II, 21 CFR 866.3830	Same
Classification Product Code	KSZ	MYR
Instrument Platform	Beckman Coulter PK7300 (BK060024)	Beckman Coulter PK7400 (BK180292)
Intended Use	Qualitative screening of blood donors for the detection of *Treponema pallidum* IgG and IgM antibodies in human serum or EDTA plasma using the Beckman Coulter PK7200 and/or PK7300 Automated Microplate Systems.	Qualitative screening of blood and plasma donors for the detection of *Treponema pallidum* IgG and IgM antibodies to syphilis in human serum, EDTA plasma or CPDA plasma using the Beckman Coulter PK7400 Automated Microplate System.
Testing Environment	Blood Donor Centers	Same
Measured Analyte	Total antibodies (IgG/IgM) to *T. pallidum*	Same
Assay Type	Qualitative	Same
Reagent Test Principle	Hemagglutination	Same
Kit Components • Reagent Cells • Sample Diluent	• Lyophilized, fixed chicken erythrocytes sensitized with components of *T. pallidum* (Nichols strain) • Phosphate buffered saline containing absorbents • Reconstituting solution	• Ready-to-use preserved avian erythrocytes coated with *T. pallidum* antigens (Nichols strain) • Saline solution containing absorbents
Reaction Vessel	Beckman Coulter Terraced Microplates	Same
Specimen Type	Human serum or EDTA plasma	Human serum, EDTA plasma or CPDA plasma

Interpretation of results	A sample where the well is non-reactive should be considered as negative for *T. pallidum.*	Same
	A sample which is reactive or indeterminate (?) in initial screening is considered as initially reactive and may be repeated in duplicate using a serum sample from the same draw.	The same algorithm except that repeat duplicate testing may be performed with the original sample (plasma or serum).
	If either duplicate is reactive or indeterminate, the sample should be considered as repeat reactive for *T. pallidum.*	Same

Characteristic	PREDICATE	PK7400 TP HA Controls PROPOSED
Controls	PK TP System Control Set BK060062	PK7400 TP HA Controls BK180301
Device Class, Regulation Code	Class II, 21 CFR 866.3830	Same
Classification Product Code	KSZ	GMR
Intended Use	For use with the PK TP System for qualitative screening of blood donors for the detection of *Treponema pallidum* IgG and IgM antibodies in human serum or EDTA plasma using the Beckman Coulter PK7200 and/or PK7300 Automated Microplate Systems.	For use with PK7400 TP HA Reagent for qualitative screening of blood and plasma donors for the detection of *Treponema pallidum* IgG and IgM antibodies to syphilis in human serum, EDTA plasma or CPDA plasma using the Beckman Coulter PK7400 Automated Microplate System.
Kit Components	Sold separately from reagent kit.	Same
• Reactive Control	Liquid human serum containing antibodies to *T. pallidum* in phosphate buffered saline	Same
• Nonreactive Control	Liquid human serum containing no detectable antibodies to *T. pallidum* in phosphate buffered saline	Normal rabbit serum containing no detectable antibodies to *T. pallidum* in phosphate buffered saline

5.7 PERFORMANCE DATA

The following performance data were provided in support of the substantial equivalence determination.

Clinical Sensitivity

Due to the low prevalence of TP reactive samples in the blood donor population, a panel of 826 commercially sourced, known TP positive samples were tested using the PK7400 TP HA Reagent on the PK7400 automated microplate system at Newmarket Biomedical in comparison with the Beckman Coulter PK TP system on the PK7300. Samples which tested initially reactive were retested in duplicate on the PK7400. The true clinical status for the commercially obtained syphilis positive samples was presumed to be that defined by the vendor assay results. In the case of discordant or concordant negative results, confirmatory testing was performed using a Syphilis Total Ab EIA.

Agreement matrix for initial testing on known serum positive samples

	PK7400		
PK7300	**IR**	**NR**	**Total**
IR	381	1	382
NR	0	0	0
Total	381	1	382

Agreement matrix for initial testing on known CPDA plasma positive samples

	PK7400		
PK7300	**IR**	**NR**	**Total**
IR	239	0	239
NR	0	0	0
Total	239	0	239

Agreement matrix for initial testing on known EDTA plasma positive samples

	PK7400		
PK7300	**IR**	**NR**	**Total**
IR	204	0	204
NR	0	1	1
Total	204	1	205

Positive percent agreement of TP HA assay on PK7400 *vs* PK7300 on initial testing

Stratified sample group	Point estimate	95% CI
Serum	99.74%	98.55 – 99.99%
CPDA	100.0%	98.47 – 100.0%
EDTA	100.0%	98.21 - 100.0%
All samples	**99.88%**	**99.33 – 100.0%**

PK7400 TP HA Reagent results comparison to clinical status for known serum positive samples after repeat testing

	PK7400		
Clinical status	**RR**	**NR**	**Total**
R	381	1	382
NR	0	0	0
Total	381	1	382

PK7400 TP HA Reagent results comparison to clinical status for known CPDA plasma positive samples after repeat testing

	PK7400		
Clinical status	**RR**	**NR**	**Total**
R	239	0	239
NR	0	0	0
Total	239	0	239

PK7400 TP HA Reagent results comparison to clinical status for known EDTA plasma positive samples after repeat testing

	PK7400		
Clinical status	**RR**	**NR**	**Total**
R	204	1	205
NR	0	0	0
Total	204	1	205

Summary of PK7400 TP HA Reagent sensitivity after repeat testing

Stratified sample group	Point estimate	95% CI
Serum	99.74%	98.55 – 99.99%
CPDA	100.0%	98.47 – 100.0%
EDTA	99.51%	97.31 – 99.99%
All samples	**99.76%**	**99.13 – 99.97%**

The rate of indeterminate (?) results for this study was 0.12% (1/826) on initial testing.

Clinical specificity

A total of 6663 random blood donor specimens (3474 EDTA plasma and 3189 serum) were tested using the PK7400 TP HA Reagent on the PK7400 automated microplate system at three major blood donor centers in the US in comparison with the Beckman Coulter PK TP system on the PK7300, their test of record for screening blood donors for antibodies to *T. pallidum.* Donor samples which tested initially reactive were retested in duplicate in both methods. Repeat reactive samples in either method were tested with FTA-ABS as a confirmatory assay. Samples that were nonreactive on repeat testing were considered true negatives for the purposes of calculating agreement.

Initial TP Results Comparison – EDTA plasma

All Sites	**Trial PK7400**		
Reference	**IR**	**NR**	**Total**
IR	0	5	5
NR	1	3468	3469
Total	1	3473	3474

Initial TP Results Comparison - serum

All Sites	**Trial PK7400**		
Reference	**IR**	**NR**	**Total**
IR	0	1	1
NR	1	3187	3188
Total	1	3188	3189

Statistical summary by sample type - Initial TP results

Sample	**All Sites**	**Agreement N=**	**Total N =**	**ROA**	**LCB**
Plasma	NPA	3468	3469	99.97%	99.84%
Serum	NPA	3187	3188	99.97%	99.83%
Combined	NPA	6655	6657	99.97%	99.89%

TP EDTA plasma results comparison – after repeat testing

All Sites	**Trial PK7400**		
Reference	**RR**	**NR**	**Total***
RR	0	0	0
NR	1	3472	3473
Total	1	3472	3473

* 1-IR on PK7300 overlooked by testing site, no additional testing performed on that donation

TP Serum results comparison – after repeat testing

All Sites	Trial PK7400		
Reference	**RR**	**NR**	**Total**
RR	0	0	0
NR	1	3188	3189
Total	1	3188	3189

Statistical summary by sample type – after repeat testing

Sample	All Sites	Agreement N=	Total* N =	ROA	LCB
Plasma	NPA	3472	3473	99.97%	99.84%
Serum	NPA	3188	3189	99.97%	99.83%

* 1-IR on PK7300 overlooked by testing site, no additional testing performed on that donation

The specificity of the subject device met the acceptance criteria.

PK7400 TP HA Reagent results comparison to clinical status for repeat testing - serum

	PK7400		
Clinical status	**RR**	**NR**	**Total**
R	1	0	1
NR	0	3188	3188
Total	1	3188	3189

PK7400 TP HA Reagent comparison results to clinical status for repeat testing – EDTA plasma

	PK7400		
Clinical status	**RR**	**NR**	**Total***
R	0	0	0
NR	1	3472	3473
Total	1	3472	3473

* 1-IR on PK7300 overlooked by testing site, no additional testing performed on that donation

The rate of indeterminate (?) results for this study was 0.015% (1/6663) on initial testing. The sample gave a repeat reactive result when retested in duplicate.

Statistical summary of PK7400 TP HA Reagent results against clinical status– after repeat testing

Sample	All Sites	Agreement N=	Total* N =	ROA	LCB
Plasma	Specificity	3472	3473	99.97%	99.84%
Serum	Specificity	3188	3188	100.0%	99.88%

* 1-IR on PK7300 overlooked by testing site, no additional testing performed on that donation.

Limit of Detection

The PK7400 TP HA Reagent has an expected limit of detection of ≤0.1 IU/mL against the WHO 1st IS for human syphilitic plasma IgG and IgM NIBSC code:05/132.

Precision

Lot to lot variability was assessed with three assay lots at one site using a panel of 826 positive and 91 negative samples.

		Agreement N=	Total N=	ROA (95%, 2-sided LCI)	Mean	SD	CV (%)
PPA	Lot 1	824	826	99.76% (99.12%)	99.80%	0.069	0.07
	Lot 2	825	826	99.88% (99.32%)			
	Lot 3	824	826	99.76% (99.12%)			
NPA	Lot 1	91	91	100% (96.27%)	100%	-	-
	Lot 2	91	91	100% (96.27%)			
	Lot 3	91	91	100% (96.27%)			

Reproducibility

Assay reproducibility was assessed at three US blood donor centers using a characterized, mixed titer panel comprising 25 syphilis positive and 5 syphilis negative samples. The panel was tested using multiple Reagent lots on 5 testing days over a 7 day period, in duplicate with two separate runs on each testing day.

Reproducibility Panel – distribution of titers for syphilis positive members

IU/mL	No of samples
0.1	5
0.2	5
0.4	5
0.8	5
1.6	5

Reproducibility study – rate of agreement

Samples	Agreement N=	Total N=	Rate of Agreement	95% CI
Syphilis positive	1500	1500	100.00%	99.75 - 100%
Syphilis negative	300	300	100.00%	98.78 - 100%
Overall	1800	1800	100.00%	99.80 - 100%

Cross reactivity

A total of 121 samples which were positive for potential cross reactants and presumed negative for syphilis were tested in the PK7400 TP HA Reagent on the PK7400 automated microplate system at Newmarket Biomedical in comparison with the Beckman Coulter PK TP system on the PK7300. Samples which tested initially reactive were retested in duplicate according to the instructions in the product IFUs. Repeat reactive samples in either method were tested in a Syphilis Total Ab EIA.

List of potential cross reacting samples

Potential cross reactant	No of samples
Toxoplasma	10
Rubella IgG	10
Lyme disease (*Borrelia sp.*)	10
SLE	10
Rheumatoid Factor	10
Epstein Barr virus (EBV)	10
HCV	10
HIV 1/2	10
HTLV	10
HBsAg	10
HAV	11
Pregnant and Multiparous	10
Total	121

PK7400 TP HA Reagent comparison to clinical status for potential cross reactants

	PK7400		
Clinical status	**RR**	**NR**	**Total**
R	1*	0	1
NR	1**	119	120
Total	2	119	121

*HIV positive sample co-infection with syphilis
**Rubella sample

	Point estimate	95% CI
PK7400 TP HA and clinical status	99.2% (120/121)	95.5 – 100%

Samples previously tested for cross reactivity in the PK7400 TP HA Reagent assay were also spiked with TP antibodies using a known positive sample. One sample from the Rubella group was excluded from the additional study as this sample had previously shown a positive result in the PK7400 assay.

22 real samples which were supplied certified as positive for both HIV and syphilis were included. A total of 132 samples were tested.

List of samples for cross reactivity study of syphilis positive samples

	Potential cross reactant	**No of samples**
Samples spiked with TP antibodies	Toxoplasma	10
	Rubella IgG	9
	Lyme disease (*Borrelia sp.*)	10
	SLE	10
	Rheumatoid Factor	10
	Epstein Barr virus (EBV)	10
	HCV	10
	HTLV	10
	HBsAg	10
	HAV	11
	Pregnant and Multiparous	10
Co-infected real samples	HIV/syphilis	22
	Total	132

	PK7400		
Expected result	**IR**	**NR**	**Total**
IR	132	0	132
NR	0	0	0
Total	132	0	132

Observed concordance level for syphilis positive samples

	Point estimate	95% Confidence Interval
PK7400 TP HA and expected result	100.0% (132/132)	97.24 – 100.0%

Sample age

Samples will be routinely tested with TP HA by the end user for up to 7 days post collection. Day 0 is date of collection. At least 900 random blood donor samples (450 EDTA plasma samples and 450 serum samples) were tested on the PK7400 at 3 US blood donor centers with a single TP HA Reagent Lot on Day 0-1 post collection and then on a minimum of 5 separate days, up to 8 days post collection, to show the ability of the TP HA and the PK7400 analyzer to produce accurate screening results for antibodies to *Treponema pallidum* from samples up to 7 days old.

Sample age – All sites plasma

Comparator (Day 1)	**Sample Age Days**	**Agreement N=**	**Total N=**	**NT N=**	**ROA**	**LCB**
PK7300	1	510	510	0	100.00%	99.28%
PK7400	1	510	510	0	100.00%	99.28%
PK7400	2	165	165	0	100.00%	97.79%
PK7400	5	180	180	0	100.00%	97.97%
PK7400	6	505	505	5	100.00%	99.27%
PK7400	7	502	502	8	100.00%	99.27%
PK7400	8	501	501	9	100.00%	99.27%

NT = No Test, results not available due to insufficient sample quantity or other data flag

All sites serum

Comparator (Day 1)	Sample Age Days	Agreement N=	Total N=	NT N=	ROA	LCB
PK7300	1	510	510	0	100.00%	99.28%
PK7400	1	510	510	0	100.00%	99.28%
PK7400	2	165	165	0	100.00%	97.79%
PK7400	5	180	180	0	100.00%	97.97%
PK7400	6	510	510	0	100.00%	99.28%
PK7400	7	504	504	6	100.00%	99.27%
PK7400	8	502	502	8	100.00%	99.27%

NT = No Test, results not available due to insufficient sample quantity or other data flag

Stability

Stability studies have been performed to support the following claims:

Reagent Kit stability
PK7400 TP HA Reagent, 18 months when stored unopened at 2-8°C.
PK7400 TP HA Sample Diluent, 24 months when stored unopened at 2-8°C.
Reagent and Sample Diluent are stable for up to 2 months once opened.

Controls kit stability
PK7400 TP HA Reactive Control, 24 months when stored unopened at 2-8°C.
PK7400 TP HA Nonreactive Control, 24 months when stored unopened at 2-8°C.
Reactive and Nonreactive Controls are stable for up to 2 months once opened.

On board stability
Reagent, Sample Diluent and Controls are stable on board the PK7400 for up to 12 hours.

Sample Stability
EDTA plasma and serum samples may be stored up to 7 days post collection at 2-8°C or up to 1 month when stored at -20°C. Samples may be subjected to 5 freeze thaw cycles at -20°C.

Interfering substances

A study was carried out to evaluate the effect of potential interfering endogenous substances. No interference was observed at the levels shown in the table below:

Substance	Maximum concentration
Human serum albumin (HSA)	120g/L
Bilirubin	0.342mmol/L
Conjugated bilirubin	0.342mmol/L
Triglyceride	37mmol/L
Intralipid	1000mg/dL
Hemoglobin	5g/L

Sample matrix

Sample matrix comparison was performed by using matched normal samples from 25 US blood donors (13 males and 12 females) which have been drawn into serum, K2 EDTA plasma and K3 EDTA plasma collection tubes and 40 matched serum and CPDA plasma samples from US blood donors.

For each donor sample, non-reactive, strong reactive and weak reactive samples were prepared for all matrices by spiking with a known syphilis positive serum. Spiked and unspiked samples were stored at 2-8°C and tested on Day 0 of the study and Day 8 to detect changes in reactivity.

Day 0 sample matrix study results

		Sample matrix		
	Result	Serum	K2 EDTA	K3 EDTA
Matched donor samples	NR	25	25	25
	R	0	0	0
Matched strong reactive samples	NR	0	0	0
	R	25	25	25
Matched weak reactive samples	NR	0	0	0
	R	25	25	25

		Sample matrix	
	Result	Serum	CPDA
Matched donor samples	NR	40	40
	R	0	0
Matched strong reactive samples	NR	0	0
	R	40	40
Matched weak reactive samples	NR	0	0
	R	40	40

Day 8 sample matrix study results

		Sample matrix		
	Result	Serum	K2 EDTA	K3 EDTA
Matched donor samples	NR	25	25	25
	R	0	0	0
Matched strong reactive samples	NR	0	0	0
	R	25	25	25
Matched weak reactive samples	NR	0	0	0
	R	25	25	25

		Sample matrix	
	Result	Serum	CPDA
Matched donor samples	NR	40	40
	R	0	0
Matched strong reactive samples	NR	0	0
	R	40	40
Matched weak reactive samples	NR	0	0
	R	40	40

100% agreement was seen at Day 0 and Day 8 for all samples.

Prozone effect

PK7400 TP HA Reagent is not affected by prozone at high levels of TP antibodies up to 100 IU/mL.

Clinical cut-off

The clinical cut-off for the PK7400 TP HA Reagent has been established as 0.025 IU/mL.

5.8 CONCLUSION

The non-clinical and clinical study data demonstrate the safety and effectiveness of the device when used for the defined indications for use and demonstrate that the device performs as well or better than the legally marketed predicate device.