510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k072115

B. Purpose for Submission:
New Device

C. Measurand:
Creatinine and Total Protein

D. Type of Test:
Quantitative, colorimetric

E. Applicant:
HORIBA ABX

F. Proprietary and Established Names:
ABX PENTRA Creatinine 120 CP reagent
ABX PENTRA Total Protein 100 CP reagent
ABX PENTRA Multical
ABX PENTRA N Control
ABX PENTRA P Control
ABX PENTRA Urine Control L/H

G. Regulatory Information:

Product Code	**Classification**	**Regulation Section**	**Panel**
alkaline picrate, colorimetry (CGX)	Class II	21 CFR 862.1225 Creatinine test system	75 Clinical Chemistry(CH)
Product Code	**Classification**	**Regulation Section**	**Panel**
biuret (colorimetric), total protein (CEK)	Class II	21 CFR§ 862.1635 Total Protein Test System	75 Clinical Chemistry(CH)
Product Code	**Classification**	**Regulation Section**	**Panel**
Calibrator, Multi-Analyte Mixture (JIX)	Class II	21 CFR 862.1150 Calibrator	75 Clinical Chemistry(CH)
Product Code	**Classification**	**Regulation Section**	**Panel**
Multi-analyte controls, all kinds (assayed and unassayed) (JJY)	Class I	21 CFR§ 862.1660 Quality control material (assayed and unassayed)	75 Clinical Chemistry(CH)

H. Intended Use:

1. Intended use(s):

   Refer to Indications for use below.

2. Indication(s) for use:
   Creatinine and Total Protein reagents, with associated calibrators and controls, are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer to measure a variety of analytes.

   ABX PENTRA Creatinine 120 CP reagent, with associated calibrator and controls, is a diagnostic reagent for quantitative in vitro determination of Creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffé method). Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

   ABX PENTRA Total Protein 100 CP reagent, with associated calibrator and controls, is a diagnostic reagent for quantitative in-vitro determination of Total Proteins in serum and plasma by colorimetry. Measurements obtained by this device are used in the diagnosis and treatment of a variety of diseases involving the liver, kidney, or bone marrow as well as other metabolic or nutritional disorders.

   The ABX PENTRA Multical is a calibrator for use in the calibration of quantitative Horiba ABX methods on Horiba ABX clinical chemistry analyzers.

   The ABX PENTRA N Control is for use in quality control by monitoring accuracy and precision.

   The ABX PENTRA Urine Control L/H is for use in quality control by monitoring accuracy and precision.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   For use with ABX PENTRA 400 Clinical Chemistry Analyzer

I. Device Description:

The ABX PENTRA Creatinine 120 CP reagent is a mono-reagent kit available in liquid form. It consists of Picric acid 10 mmol/l, Sodium hydroxide 260 mmol/L, and Surfactants pH 13.0 ± 0.2 at 25°C.

ABX PENTRA Total Protein 100 CP reagent is ready use mono-reagent kit in liquid format. It consists of Copper II Sulphate 12 mmol/l, Potassium Sodium Tartrate 32 mmol/L, Potassium Iodide 30 mmol/L, Sodium Hydroxide 600 mmol/l pH 13.5 ± 0.1 at 20°C.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   InfinityTM Creatinine Liquid Stable Reagent; Creatinine

2. Predicate 510(k) number(s):
k973869; k941837

3. Comparison with predicate:

ABX PENTRA Creatinine 120 CP reagent – Serum/Plasma

Item	Predicate Device (k973869) InfinityTM Creatinine Liquid Stable Reagent	New Device ABX Pentra Creatinine 120 CP
Analyte	Creatinine	Creatinine
Method	Colorimetric test using alkaline picrate (Jaffe reaction)	Identical
Sample Matrix	Serum	Serum, Plasma, Urine
Linearity/Assay range	Serum: 0 mg/dl – 20 mg/dL	Serum/Plasma: 0.18 mg/dl – 22.60 mg/dL
Detection Limit	-	0.18 mg/dL
Closed reagent stability	Until the expiration date when stored at 2-8°C	24 months at 2-8°C
Open reagent (on-board) stability	Until the expiration date when stored at 2-8°C	10 days
Calibrator stability	N/A	24 hours

ABX PENTRA Creatinine 120 CP reagent – Urine

Item	Predicate device (k941837) Creatinine	New Device ABX Pentra Creatinine 120 CP
Analyte	Creatinine	Creatinine
Method	Kinetic method using alkaline picrate (modification of the Jaffé reaction)	Colorimetric test using alkaline picrate (Jaffe reaction)
Sample Matrix	Serum, Plasma, Urine	Serum, Plasma, Urine
Linearity/Assay range	Urine: Upto 2000 mg/dL	Urine: 1.39 mg/dl – 282.5 mg/dl; with automatic post-dilution: 857.5 mg/dL
Detection Limit	-	1.39 mg/dL
Closed reagent stability	Until the expiration date when stored at 2-8°C	24 months at 2-8°C
Open reagent (on-board) stability	Until the expiration date when stored at 2-8°C	10 days
Calibrator stability	N/A	24 hours

ABX PENTRA Total Protein 100 CP

Item	Predicate device (k973869): Total Protein Reagent Biuret Method	New Device ABX Pentra Total Protein 100 CP
Analyte	Total Protein	Total Protein
Method	Colorimetric test using copper ions in alkaline solution, with the addition of tartrate (enhanced Biuret reaction)	Identical
Sample Matrix	Serum, Plasma	Serum, Plasma
Linearity/Assay range	0 g/dl - 15 g/dL	0.1 g/dl – 10.0 g/dL
Detection Limit	-	0.01 g/dL
Closed reagent stability	Until the expiration date when stored at 2-25°C	26 months at 2-25°C
Open reagent (on-board) stability	Until the expiration date when stored at 2-8°C	14 days
Calibrator stability	N/A	24 hours

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

- CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Second Edition
- CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.
- CLSI EP17-A: Protocol for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.
- CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition.

L. Test Principle:

ABX PENTRA Creatinine 120 CP reagent: Creatinine reacts with alkaline picrate to produce a reddish component (Jaffé reaction). The red color obtained, which is measured at 500 nm by spectrophotometry is directly proportional to the creatinine concentration present in the sample.

ABX PENTRA Total Protein 100 CP: The peptide bonds of protein react with the copper II ions in alkaline solution to form a blue-violet complex (the biuret reaction), each copper ion complexing with 5 or 6 peptides bonds (2). Tartrate is added as a stabilizer while iodide is used to prevent auto-reduction of the alkaline copper complex. The color formed is proportional to the protein concentration and is measured at 520-560 nm.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

For ABX PENTRA Creatinine 120 CP reagent, within run precision was evaluated for serum using 2 controls and 3 serum specimens tested 20 times in a single run for each sample. In accordance with the CLSI document, EP05-A, the sponsor tested the same 3 specimens and 2 controls in duplicate for 20 days with two series per day (80 data points). The results are given below.

Specimen	Level (mg/dL)	Within-Run		Between Run		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)
N Control	1.09	0.03	2.66	0.03	3.19	0.06	5.83
P Control	3.75	0.02	0.64	0.05	1.44	0.07	1.85
Serum 1	0.59	0.02	3.03	0.02	3.47	0.03	5.78
Serum 2	1.67	0.02	1.23	0.03	1.81	0.05	2.99
Serum 3	7.00	0.03	0.43	0.09	1.32	0.11	1.55

For ABX PENTRA Creatinine 120 CP reagent on urine samples, within run precision was evaluated using 2 controls (Control L/H) and 3 urine specimens tested 20 times in a single run for each sample. In accordance with the CLSI document, EP05-A, the sponsor tested the same 3 specimens and 2 controls in duplicate for 20 days with two series per day (80 data points). The results are given below.

Specimen	Level (mg/dL)	Within-Run		Between Run		Total	
		SD	CV(%)	SD	CV (%)	SD	CV (%)
Control L	60.5	0.55	0.91	0.95	1.56	1.25	2.07
Control H	129.1	0.74	0.58	1.79	1.39	2.38	1.85
Urine 1	12.7	0.44	3.44	0.44	3.48	0.76	6.00
Urine 2	100.9	0.56	0.56	1.28	1.27	1.87	1.85
Urine 3	245.6	1.06	0.43	2.99	1.22	4.36	1.78

For ABX PENTRA Total Protein 100 CP reagent, within run precision was evaluated for serum using 2 controls and 3 serum specimens tested 20 times in a single run for each sample. In accordance with the CLSI document, EP05-A, the sponsor tested the same 3 specimens and 2 controls in duplicate for 20 days with two series per day (80 data points). The results are given below.

Specimen	Level (mg/dL)	Within-Run		Between Run		Total	
		SD	CV (%)	SD	CV (%)	SD	CV (%)
N Control	67.8	0.51	0.75	0.81	1.19	0.95	1.41
P Control	51.3	0.56	1.10	0.56	1.10	0.80	1.55
Serum 1	41.1	0.48	1.16	0.43	1.05	0.64	1.56
Serum 2	64.4	0.56	0.87	0.54	0.84	1.04	1.62
Serum 3	88.8	0.48	0.54	0.83	0.93	1.13	1.27

b. *Linearity/assay reportable range*:

The sponsor conducted linearity studies in accordance with CLSI EP6-A. For ABX PENTRA Creatinine 120 CP reagent for serum samples, the sponsor used an in house preparation of aqueous creatinine solution diluted to generate 11 concentrations (mean values of the range 0.228 – 28.492 mg/dL). The sponsor's acceptance criterion for the bias with linearity is ± 8%. Each test level was run in four repeats on Pentra 400 analyzer. Based on a linear regression analysis conducted for measured and assigned values, the assay was shown to be linear within the entire range tested. Based on these results as well as Limit of detection studies below, the sponsor established the assay reportable range for serum/plasma at 0.18 – 22.60 mg/dL. The sponsor also conducted post dilution linear range studies to establish serum values above the upper limit of 22.60 mg/dL. The goal of this study was to compare manual dilution with the automatic dilution performed by the Pentra 400. Based on the sponsors' internal acceptance criteria of ± 10% recovery (manual vs. automatic dilution), the sponsor established the upper limit of 67.8 mg/dL for the extended range.

The sponsor conducted a similar study for ABX PENTRA Creatinine 120 CP reagent for urine samples using an in house preparation (concentration range: 5.20 – 362.84 mg/dL) and each of the 11 concentration level tested in four repeats. Based on a linear regression analysis conducted for measured and assigned values, the assay was shown to be linear within the entire range tested. Based on these results as well as Limit of detection studies below, the sponsor established the assay reportable range for urine at 1.39 – 282.50 mg/dL. The sponsor also conducted post dilution linear range studies to establish urine values above the upper limit of 282.50 mg/dL. The goal of this study was to compare manual dilution with the automatic dilution performed by the Pentra 400. Based on the sponsors' internal acceptance criteria of ± 10% recovery (manual vs. automatic dilution), the sponsor established the upper limit of 857.5 mg/dL for the extended range.

The sponsor conducted similar study for ABX PENTRA Total Protein 100 CP reagent for serum using an in house sera preparation diluted to generate 11 concentrations (mean values of the range 0.997 – 11.678 g/dL) with each concentration level tested in four repeats. Based on a linear regression analysis conducted for measured and assigned values, and in accordance with the sponsor's acceptance criteria of the bias within ± 4%, the assay was shown to be linear within the entire range tested. Based on these results as well as Limit of detection studies below, the sponsor established the assay reportable range for serum total protein at 0.1 – 10.0 g/dL. The sponsor also conducted post dilution linear range studies to establish serum total protein values above the upper limit of 10 g/dL. The goal of this study was to compare manual dilution with the automatic dilution performed by the Pentra 400. Based on the sponsors' internal acceptance criteria of ± 10% recovery (manual vs. automatic dilution), the sponsor established the upper limit of 20.0 g/dL for the extended range.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The calibrators and controls used in this submission are previously cleared. The creatinine and total protein material introduced in to the calibrators and their

corresponding values are traceable to reference material SRM909b and SRM927C/Verichem 9460, respectively. The assigned value is the median of all the values generated for each calibrator and control. Additionally, control range is calculated as the target value ± 3 standard deviations. Please refer to the value assignment sheet in the labeling for lot-specific values.

The sponsor conducted stability studies for the reagents and calibrators and controls. Based on the acceptance criteria of the material recovery is within target value ± 10%, the sponsor claims shelf life of 24 months, open-vial stability of 4 months, and on-board stability of 10 days for ABX PENTRA Creatinine 120 CP reagent. For ABX PENTRA Total Protein 100 CP reagent, the sponsor claims shelf life of 26 months and on-board stability of 14 days. To ensure adequate quality control, the sponsor recommends calibrating the test everyday and every time a new reagent bottle is used. The sponsor also recommends using quality control samples at least once a day, after each calibration and when a new bottle is used. However, the sponsor also suggests the control intervals must be adapted to the individual laboratory requirement.

d. *Detection limit:*

The sponsor evaluated Limit of Detection (LoD) and Limit of Blank (LoB) for ABX PENTRA Creatinine 120 CP reagent for serum and urine samples and ABX PENTRA Total Protein 100 CP reagent for serum on Pentra 400 instrument following the guidelines in CLSI EP17-A. Results were evaluated for Gaussian distribution and LoB values generated using parametric procedure. LoB was determined using physiological water (0.9% NaCl) assayed 201 (Creatinine 120 CP reagent for serum), 120 (Creatinine 120 CP reagent for urine), and 60 (Total Protein 100 CP reagent for serum) times on 3 Pentra 400 instruments with the method in evaluation. The LoB values were, 0.106 mg/dL, 0.01 mg/dL, and -0.008 g/dL, respectively.

To determine the LoD, the sponsor used four samples with concentrations between LoB and LoB x 5 and assayed 20 times. Results were evaluated for Gaussian distribution and LoD values generated using parametric procedure. LoD values for Pentra 400 instrument were, 0.177 mg/dL for Creatinine 120 CP reagent for serum, 1.39 mg/dL for Creatinine 120 CP reagent for urine, and 0.01 g/dL for Total Protein 100 CP reagent for serum.

e. *Analytical specificity:*

For ABX PENTRA Creatinine 120 CP reagent for serum and urine, the sponsor evaluated the effect of hemoglobin (0-259 mg/dL), direct bilirubin (0 – 26 mg/dL), total bilirubin (0-33 mg/dL), lipemia (intralipid) (0-613 mg/dL), glucose (15 g/L) and total protein (122 g/L) on pooled sera at two creatinine concentrations (low and high) spiked with the interferents, and then compared with unspiked control. Based on the sponsor-defined interference limit of ± 10% of control, the following interference limit claims were set by the sponsor for each reagent set.

Interference results at 1 mg/dL creatinine

Interferent	**No Interference (±10%) claim**	
	Serum	*Urine*
Hemoglobin (mg/dL)	259	259
Lipemia (mg/dL)	612.5	612.5
Direct bilirubin (mg/dL)	8.1	14.6
Total Bilirubin (mg/dL)	16.9	-
Glucose (g/L)	11.7	-
Total protein (g/L)	122	-

For ABX PENTRA Total Protein 100 CP reagent for serum, the sponsor evaluated the effect of hemoglobin (0-241 mg/dL), direct bilirubin (0 – 29 mg/dL), total bilirubin (0-29 mg/dL), and lipemia (intralipid) (0-613 mg/dL) on pooled sera at two creatinine concentrations (low and high) spiked with the interferents, and then compared with unspiked control. Based on the sponsor-defined interference limit of ± 10% of control, the interference limit claims were, lipemia (437 mg/dL), total bilirubin (29.3 mg/dL), and direct bilirubin (21.9 mg/dL). The sponsor recommended not using hemolyzed samples.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison studies were conducted in accordance with CLSI EP9-A2 guidelines. Performance of the ABX PENTRA Creatinine 120 CP reagent for serum was compared with the predicate device, InfinityTM Creatinine Liquid Stable Reagent (k973869). A total of 122 serum samples (range: 0.55 – 22.06 mg/dL) were used. Data analysis was done using linear regression and Passing-Bablock regression. The data demonstrated the device is substantially equivalent to the predicate device based on linear regression ($y = 0.977x + 0.005$; $r = 0.999$) and Passing-Bablock regression ($y = 0.98x - 0.04$; $r = 1.0$). Performance of the ABX PENTRA Creatinine 120 CP reagent for urine was compared with the predicate device, Creatinine reagent (k941837). A total of 119 urine samples (range: 7.1 – 303 mg/dL) were used. Data analysis was done using linear regression and Passing-Bablock regression. The data demonstrated the device is substantially equivalent to the predicate device based on linear regression ($y = 0.9538x - 0.2488$; $r = 0.9975$) and Passing-Bablock regression ($y = 0.96x - 0.73$; $r = 1.0$).

Performance of the ABX PENTRA Total Protein 100 CP reagent for serum was compared with the predicate device, Total Protein Reagent (k973869). A total of 178 serum samples (range: 1.01 – 9.38 g/dL) were used. Data analysis was done using linear regression and Passing-Bablock regression. The data demonstrated the device is substantially equivalent to the predicate device based on linear regression ($y = 1.0203x - 0.118$; $r = 0.9921$) and Passing-Bablock regression ($y = 1.03x - 0.20$; $r = 1.0$).

b. Matrix comparison:

To demonstrate comparable performance between serum and lithium-heparin or EDTA plasma, the sponsor compared 70 samples ranging from 0.31 mg/dL to 20.02 mg/dL for the ABX PENTRA Creatinine 120 CP reagent and 70 samples ranging from 1.30 g/dL to 9.81 g/dL for the ABX PENTRA Total Protein 100 CP reagent using PENTRA 400 analyzer. Linear regression analysis for ABX PENTRA Creatinine 120 CP reagent yielded linear regression equations for lithium-heparin ($y = 0.971x + 0.032$; $r = 0.999$) and EDTA plasma ($y = 0.976x + 0.032$; $r = 0.997$). The sponsor claimed no significant differences between serum and plasma. Similarly, for ABX PENTRA Total Protein 100 CP reagent linear regression analysis yielded linear regression equations for lithium-heparin ($y = 0.953x + 0.117$; $r = 0.999$) and EDTA plasma ($y = 0.977x - 0.1586$; $r = 0.991$). The sponsor claimed no significant differences between serum and plasma.

3. Clinical studies:

a. Clinical Sensitivity:
Not Applicable

b. Clinical specificity:
Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):
Not Applicable

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range:

The expected values of creatinine and total proteins are based on literature*. The expected values for total protein in blood are 6.0 – 7.8 g/dL. The expected values for creatinine in blood for males and females are, 0.8 – 1.3 mg/dL and 0.6 – 1.2 mg/dL, respectively. The expected values for creatinine in urine for males and females are, 14 - 26 mg/kg/day and 11 - 20 mg/kg/day, respectively.

* Tietz NW. Clinical Guide to Laboratory Tests. 4th ed. St. Louis, MO: WB Saunders Company; 2006.

N. Proposed Labeling:
The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

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