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

A. 510(k) Number:

k110530

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, colorimetric

E. Applicant:

Horiba ABX S.A.S

F. Proprietary and Established Names:

ABX PENTRA Creatinine 120 CP reagent

ABX PENTRA Multical

ABX PENTRA N Control

ABX PENTRA P Control

ABX PENTRA Urine Control L/H

G. Regulatory Information:

1. Regulation section:

Product Code	Classification	Regulation Section	Panel
CGX, alkaline picrate, colorimetry	Class II	21 CFR 862.1225 Creatinine test system	75 Clinical Chemistry
Product Code	**Classification**	**Regulation Section**	**Panel**
JIT, Calibrator, multi-analyte mixture	Class II	21 CFR 862.1150 Calibrator	Clinical Chemistry (75)
Product Code	**Classification**	**Regulation Section**	**Panel**
JJX, Multi-analyte controls	Class I, reserved	21 CFR 862.1660 Quality control material (assayed and unassayed)	Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See Indications for use in (2) below

2. Indication(s) for use:

   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.

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

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

   The ABX PENTRA P 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 bi-reagent cassette available in liquid form. It consists of sodium hydroxide 0.25 mol/L in Reagent 1 and picric acid 20.5 mmol/L in Reagent 2.

The ABX PENTRA Multical is a lyophilized human serum calibrator with chemical additives and materials of biological origin. The assigned values of the calibrator components are given in the product labeling, ensuring optimal calibration of the appropriate HORIBA ABX SAS methods on the ABX PENTRA 400 analyzer. This calibrator is provided in ten vials of 3 mL.

The **ABX PENTRA N Control** and **ABX PENTRA P Control** are quality control products consisting of lyophilized human serum with chemical additives and materials of biological origin added as required to obtain given component levels. The assigned values of the control components are given in the product labeling, ensuring control of the appropriate HORIBA ABX SAS methods on the ABX PENTRA 400 analyzer. Each control is provided in ten vials of 5 mL.

The **ABX PENTRA Urine Control L/H** is a two-level (Low and High) quality control consisting of liquid solutions prepared from human urine with chemical additives and materials of biological origin added as required to obtain given component levels. The assigned values of the control components are given in the product labeling, ensuring control of the appropriate HORIBA ABX SAS methods on the ABX PENTRA 400 analyzer. Each control level is provided in one vial of 10 mL.

The sponsor stated in the labeling that each donor unit used in the preparation of the calibrator and controls were tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to Hepatitis C (HCV) and antibody to HIV-I/HIV-2.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   CREATININE REAGENT OLYMPUS

   ABX PENTRA Multical; ABX PENTRA Control N and P; ABX PENTRA Urine Control L/H

2. Predicate 510(k) number(s):
   k934361, k052007, k070249

3. Comparison with predicate:

Similarities and Differences		
Item	ABX Pentra Creatinine 120 CP Reagent	Olympus Creatinine Reagent
Indications for Use	for quantitative in vitro determination of Creatinine in human serum, plasma and urine. 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.	same
Test method	Jaffe kinetic method	same
Measuring range	Serum/plasma: 0.22 to 18.08 mg/dL Urine: 2.90 to 282.50 mg/dL	Serum/plasma: 0.20 to 25.0 mg/dL Urine: 1 to 300 mg/dL

Items	ABX PENTRA Multical (Candidate Device)	ABX PENTRA Multical (k072115)
Intended use/Indication for use	Same	For use in the calibration of quantitative Horiba Medical methods on Horiba Medical clinical chemistry analyzers.
Matrix	Same	Lyophilized human serum with chemical additives
Analytes	addition of Creatinine CP	Multi-analyte calibrator

Items	ABX PENTRA Control N and P (Candidate Device)	ABX PENTRA Control N and P (k072115)
Intended use/Indication for use	Same	For use in quality control by monitoring accuracy and precision.
Matrix	Same	Lyophilized human serum with chemical additives
Analytes	addition of Creatinine CP	Multi-analyte control material

Items	ABX PENTRA Urine Control L/H (Candidate Device)	ABX PENTRA Urine Control L/H (k072115)
Intended use/Indication for use	Same	For use in quality control by monitoring accuracy and precision.
Matrix	Same	Human urine with chemical additives
Analytes	addition of Creatinine CP	Multi-analyte control material

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline

CLSI EP6-A: Evaluation of Linearity of Quantitative Measurement Procedures, A Statistical Approach: Approved Guideline

CLSI EP9-A: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline

CLSI EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

L. Test Principle:

ABX PENTRA Creatinine 120 CP reagent: Creatinine reacts with alkaline picrate to form Janousky complex. The rate of increase in the absorbance at 510 nm due to the formation of creatinine-picrate complex is directly proportional to the creatinine concentration present in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

    a. *Precision/Reproducibility:*

    For ABX PENTRA Creatinine CP reagent, within run precision was evaluated for serum using 2 controls and 4 serum specimens tested 20 times in a single run for each sample. In accordance with the CLSI document, EP05-A, the sponsor tested 3 specimens and 2 controls in duplicate for 20 days with two series per day (n =80) on one ABX PENTRA 400 analyzer using one lot of reagent. The results are given below:

Specimen	Level (mg/dL)	Within-run		Level (mg/dL)	Total	
		SD	CV%		SD	CV%
Control 1	1.15	0.020	1.74	1.16	0.04	3.47
Control 2	4.01	0.066	1.64	4.14	0.09	2.17
Specimen 1	0.61	0.010	1.61	0.71	0.03	4.72
Specimen 2	1.73	0.030	1.74	2.06	0.05	2.46
Specimen 3	7.79	0.141	1.82	7.31	0.17	2.36
Specimen 4	14.57	0.177	1.33			

For ABX PENTRA Creatinine 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 (n = 80) on one ABX PENTRA 400 analyzer using one lot of reagent. The results are given below:

Specimen	Level (mg/dL)	Within-run		Level (mg/dL)	Total	
		SD	CV%		SD	CV%
Control L	63.3	0.074	1.16	63.0	1.36	2.16
Control H	140.1	1.39	0.99	137.3	2.88	2.10
Urine 1	12.7	0.2	1.55	12.6	0.025	1.99
Urine 2	104.6	0.88	0.84	105.4	2.03	1.92
Urine 3	260.2	2.43	0.93	261.6	5.38	2.06

b. *Linearity/assay reportable range:*

Linearity was evaluated following CLSI guideline EP6-A. For serum linearity, a spiked serum sample was used as the high sample and a diluted serum sample was used as the low sample. The intermediate concentrations consisted of dilutions of the high and low sample to obtain 10 levels with values ranging from 0.22 to 29.31 mg/dL. For urine creatinine linearity, a spiked urine sample was used as the high sample and a 0.9% saline sample was used as the low sample. Ten levels with values up to 459 mg/dL were tested. For both studies, the mean of 4 replicate measurements were used in the regression analyses. The linear regression equation for serum was $y = 1.066x + 0.0269$. For urine the linear regression equation was $y = 0.9962x - 0.08$.

Based on the results of the linearity study and the limit of detection studies (see below in d), the sponsor claimed that the reportable range for serum is 0.22 – 18.08 mg/dL and for urine is 2.9 – 282.5 mg/dL. The sponsor has also provided data to support that automatic dilution can go up to 54.24 mg/dL for serum and 847.5 mg/dL for urine.

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

The calibrators and controls used in this submission are previously cleared in k052007 for ABX PENTRA Multical, ABX PENTRA N Control and ABX PENTRA P Control and in k070249 for ABX PENTRA Urine Control L/H. The creatinine material introduced in to the calibrators and its corresponding value is traceable to NIST reference material SRM967. In this submission, creatinine values for this assay for urine and serum/plasma are being added to the existing calibrator and control materials. The assigned target value for the Multical calibrator is the median of all the results generated for each calibrator based on 150 measurements on 6 analyzers. The control ranges are calculated as the target value ± 3 standard deviations (based on 150 measurements on 6 instruments). Please refer to the value assignment sheet in the labeling for lot-specific values.

Real-time testing was conducted to establish the stability of the calibrator and control materials. The stability study protocol and the acceptance criteria have been reviewed and found to be acceptable. The study results support the following stability claims in the labeling:

Closed-Vial and Open-Vial Stability

Item	Storage Conditions		Claimed Stability
Reagent Packs	Close-Vial	2-8°C	36 months
	Open-Vial	On system, 2-8°C	19 days
Calibrators	Close-Vial	2-8°C	24 months
	Open-Vial	-25 °C to -15°C	2 weeks
		2-8°C	2 days
		15°C to 25°C	8 hours
Serum controls	Close-Vial	2-8°C	30 months
	Open-Vial	-25 °C to -15°C	1 month
		2-8°C	5 days
		15°C to 25°C	12 hours
Urine Controls	Close-Vial	2-8°C	24 months
	Open-Vial	2-8°C	30 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.

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 following the guidelines in CLSI EP17-A. LoB was determined using physiological water (0.9% NaCl) assayed 90 times each for Creatinine 120 CP

reagent for serum and Creatinine 120 CP reagent for urine using 3 PENTRA 400 instruments. The LoB values were 0.01mg/dL, and 1.0 mg/dL respectively.

To determine the LoD, the sponsor used four altered serum or urine samples with concentrations between LoB and LoB x 4 which were assayed 20 times for each sample. LoD values were 0.03 mg/dL for Creatinine 120 CP reagent for serum and 1.4 mg/dL for Creatinine 120 CP reagent for urine.

To determine the LoQ, the sponsor tested a range of low concentration serum and urine samples 10 times. The % CV and bias vs. the actual concentrations were calculated. The LoQ was the lowest concentration sample where the % CV was lower than 15% and the relative bias was inside the +/- 10% range. The LoQ for serum creatine was determined to be 0.22 mg/dL. The LoQ for urine creatinine was determined to be 2.9 mg/dL.

e. *Analytical specificity:*

For ABX PENTRA Creatinine 120 CP reagent for serum and plasma, the sponsor evaluated the effect of hemoglobin, direct bilirubin, total bilirubin, lipemia (as triglyceride), glucose, ascorbic acid and total protein on pooled sera at two creatinine concentrations (low and high) spiked with the interferents, and then compared with unspiked control. Based on the sponsor's definition of no significant interference as ≤ 10% of control, the following interference limit claims were set by the sponsor for each reagent:

Serum/plasma

Hemoglobin: no significant interference up to 500 mg/dL

Triglyceride: no significant interference up to 516 mg/dL

Total bilirubin: no significant interference up to 29.3 mg/dL

Direct bilirubin: no significant interference up to 19.9 mg/dL

Glucose: no significant interference up to 233 mg/dL

Ascorbic acid: no significant interference up to 5.98 mg/dL

Urine

Hemoglobin: no significant interference up to 362 mg/dL

Triglyceride: no significant interference up to 612.5 mg/dL

Direct bilirubin: no significant interference up to 29.3 mg/dL

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, Olympus/Beckman Creatinine Reagent (k934361). A total of 165 serum samples (range: 0.45- 16.72 mg/dL) were used. Data analysis was done using Passing-Bablok regression. The data demonstrated the device is substantially equivalent to the predicate device based on Passing-Bablok regression (y = 0.99x + 0.03 [95% CI = 0.98 – 0.99]; r^2 = 0.9984).

   Performance of the ABX PENTRA Creatinine 120 CP reagent for urine was compared with the predicate device, Olympus/Beckman Creatinine Reagent (k934361). A total of 117 urine samples (range: 3.9 – 273 mg/dL) were used. Data analysis was done using Passing-Bablok regression. The data demonstrated the device is substantially equivalent to the predicate device based on Passing-Bablok regression (y = 1.00x -0.60 [95% CI = 0.99 – 1.01]; r^2 = 0.9984).

   b. *Matrix comparison:*

   To demonstrate comparable performance between serum and lithium-heparin or EDTA plasma, the sponsor compared 40 samples ranging from 0.52 mg/dL to 15.94 mg/dL for the ABX PENTRA Creatinine 120 CP using PENTRA 400 analyzer. Linear regression analysis for ABX PENTRA Creatinine 120 CP reagent yielded linear regression equations for lithium-heparin (y = 0.9942x +0.0275; r = 1.000) and EDTA plasma (y = 1.0409x -0.0119; r = 1.000).

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):

4. Clinical cut-off**:**

   See expected values in (5) below

5. Expected values/Reference range:

   The expected values of creatinine are based on literature*. 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.