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

A. 510(k) Number:

k070249

B. Purpose for Submission:

To expand the indications for use with urine and to add urine control materials

C. Measurand:

Amylase, calcium, creatinine, and phosphorus

D. Type of Test:

Quantitative

E. Applicant:

HORIBA ABX

F. Proprietary and Established Names:

ABX PENTRA Amylase CP, ABX PENTRA Calcium CP, ABX PENTRA Creatinine CP, ABX PENTRA Phosphorus CP, and ABX PENTRA Urine Control L/H

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1070: Amylase Test System, 862.1145: Calcium Test System, 862.1225: Creatinine Test System, 862.1580: Phosphorus (inorganic) Test System, and 862.1660: Quality Control Material (assayed and unassayed)

2. Classification:

   Class II: Amylase, Calcium, and Creatinine
   Class I, reserved: QC Material
   Class I: Phosphorus

3. Product codes:

JFJ – Catalytic Methods, Amylase; CIC – Cresolphthalein Complexone, Calcium; CGX – Alkaline Picrate, Colorimetry, Creatinine; CEO – Phosphomolybdate (colorimetric), Inorganic Phosphorus; and JJY – Multi-Analyte Controls, All Kinds (Assayed and Unassayed)

4. Panel:

   Chemistry (75)

H. Intended Use:

1. Intended uses:

   See Indications for use below.

2. Indications for use:

   ABX PENTRA Amylase CP reagent with associated calibrators and controls are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer for quantitative in vitro diagnostic determination of the activity of the enzyme amylase in human serum, plasma and urine based on an enzymatic photometric assay. Amylase measurements are used in the diagnosis and treatment of pancreatitis (inflammation of the pancreas).

   ABX PENTRA Calcium CP reagent with associated calibrators and controls are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer for quantitative in vitro diagnostic determination of calcium in human serum, plasma and urine based on a photometric test using orthocresolphtalein complexone. Calcium measurements are used in the diagnosis and treatment of parathyroid disease, a variety of bone diseases, chronic renal disease and tetany (intermittent muscular contractions or spasms).

   ABX PENTRA Creatinine CP reagent with associated calibrators and controls are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer for quantitative in vitro diagnostic determination of creatinine in human serum, plasma and urine based on a kinetic method using alkaline picrate (Jaffe' 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 Phosphorus CP reagent with associated calibrators and controls are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer for quantitative in vitro diagnostic determination of creatinine in human serum, plasma and urine based on a UV method using phosphomolybdate. Measurements of phosphorus (inorganic) are used in the diagnosis and treatment of various disorders, including parathyroid gland and kidney diseases, and vitamin D imbalance.

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

3. Special conditions for use statement(s):

   The device is for prescription use.

4. Special instrument requirements:

   ABX PENTRA 400 Clinical Chemistry Analyzer

I. Device Description:

The **ABX PENTRA Amylase CP** is composed of a bi-reagent cassette with 26 mL and 6.5 mL compartments. Reagent 1 consists of Good's buffer, NaCl, $MgCl_2$, α-Glucosidase, and sodium azide. Reagent 2 consists of Good's buffer, EPS-G7, and sodium azide.

The **ABX PENTRA Calcium CP** is composed of a bi-reagent cassette with 66 mL and 16.5 mL compartments. Reagent 1 consists of ethanolamine and detergents. Reagent 2 consists of o-Cresolphthalein complexone, 8-Hydroxyquinoline, and hydrochloric acid.

The **ABX PENTRA Creatinine CP** is composed of a bi-reagent cassette with two 28 mL compartments. Reagent 1 consists of picric acid, and Reagent 2 consists of sodium hydroxide and disodium phosphate.

The **ABX PENTRA Phosphorus CP** is composed of a mono-reagent cassette with a 29.5 mL compartment. The reagent consists of sulfuric acid and ammonium molybdate.

The **ABX PENTRA Urine Control L/H** is a liquid prepared from human urine with added constituents of human and animal origin, chemicals, preservatives, and stabilizers. The set is composed of 2 vials: 1 vial of low control (10 mL) and 1 vial of high control (10 mL).

All reagents are supplied ready-to-use.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Infinity™ Amylase Liquid Stable Reagent, Roche Calcium, Roche Creatinine, Roche Inorganic Phosphorus, and Liquichek™ Urine Chemistry Control

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

   k972297, k896224, k941837, k883962, and k020817

3. Comparison with predicate:

Amylase		
Item	Device	Predicate
Intended Use	Quantitative determination of α-amylase in serum, plasma and urine	Quantitative determination of α-amylase in human serum or urine
Methodology	Enzymatic photometric assay	Same
Measuring Range	4.92 to 2000 U/L	10 to 2000 U/L

Calcium		
Item	Device	Predicate
Intended Use	Quantitative determination of calcium in serum, plasma and urine	Quantitative measurement of calcium in serum, heparinized plasma, or urine
Methodology	Photometric test using orthocresolphthalein complexone	Same
Measuring Range	0.12 to 24.06 mg/dL	0.08 to 15.0 mg/dL

Creatinine		
Item	Device	Predicate
Intended Use	Quantitative determination of creatinine in serum, plasma and urine	Quantitative determination of creatinine in serum, plasma, and urine
Methodology	Kinetic method using alkaline picrate (modification of the Jaffe' reaction)	Same
Measuring Range	1.3 to 316.4 mg/dL	Up to 200 mg/dL

Phosphorus		
Item	Device	Predicate
Intended Use	Quantitative determination of phosphorus in serum, plasma and urine	Quantitative determination of inorganic phosphorus in serum and urine
Methodology	UV method using phosphomolybdate	Same

Phosphorus		
Item	Device	Predicate
Measuring Range	1.28 to 198.4 mg/dL	Up to 150 mg/dL

Urine Control		
Item	Device	Predicate
Intended Use	Monitoring accuracy and precision for the methods below	Monitoring the precision of laboratory testing procedures for the analytes below
Matrix	Human urine with added constituents of human and animal origin, chemicals, preservatives and stabilizers	Same
Analytes	Amylase, calcium, creatinine, and phosphorus	Amylase, calcium, chloride, cortisol, creatinine, glucose, human chorionic gonadotropin, magnesium, microalbumin (albumin), osmolality, pH, phosphorus, potassium, sodium, specific gravity, urea, urea nitrogen, and uric acid
Format	Liquid	Same
Levels	Two levels	Same

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

- EP5-A2 – Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition
- EP6-A – Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline
- EP9-A2 – Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition
- EP21-A – Evaluation of Total Analytical Error for Clinical Laboratory Methods; Approved Guideline
- Guidance for Industry and FDA Staff: "Format for Traditional & Abbreviated 510(k)s": August 12, 2005
- "Guidance for Industry and FDA Staff Bundling Multiple Devices or Multiple Indications in a Single Submission, November 2003"

- "Guidance for Industry – In vitro diagnostics Creatinine Test System July 1998"
- "In vitro diagnostic devices: Guidance for the preparation of 510(k) submissions Jan 1997"

L. Test Principle:

The **amylase** assay is based on an enzymatic photometric test. The **calcium** assay is based on a photometric test using orthocresolphthalein complexone. The **creatinine** assay is based on a kinetic method using alkaline picrate (Jaffe' method). The **phosphorus** assay is based on a UV method using phosphomolybdate.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Amylase:

To evaluate within run precision, ABX Pentra Urine Control L/H (level 1 & 2) and three human urine specimens were tested 20 times in a single run for each sample, per the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745). The results found were as follows:

U/L	**Control L**	**Control H**	**Sample 1**	**Sample 2**	**Sample 3**
Mean	44.7	169.4	86.4	157.7	286.8
%CV	3.16	1.14	1.65	0.63	0.63

To evaluate between run and total precision, ABX Pentra Urine Control L/H (level 1 & 2) and three human urine specimens were tested in duplicate for 20 days, two series per day, per the CLSI document, EP5-A. The results found were as follows:

U/L	**Control L**	**Control H**	**Sample 1**	**Sample 2**	**Sample 3**
Mean	53.98	163.45	46.79	135.54	394.54
%CV					
Total	4.29	1.51	6.03	3.96	3.19
Between Day	2.01	1.04	5.19	3.56	3.02
Between Run	2.67	0.68	1.78	1.34	0.94

Calcium:

To evaluate within run precision, ABX Pentra Urine Control L/H (level 1 & 2) and three human urine specimens were tested 20 times in a single run for each sample, per

the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745). The results found were as follows:

	Control L	Control H	Sample 1	Sample 2	Sample 3
Mean (mmol/L)	2.39	3.56	1.11	2.51	4.10
Mean (mg/dL)	9.57	14.29	4.44	10.05	16.43
%CV	1.83	0.54	1.00	0.84	0.96

To evaluate between run and total precision, ABX Pentra Urine Control L/H (level 1 & 2) and three human urine specimens were tested in duplicate for 20 days, two series per day, per the CLSI document, EP5-A. The results found were as follows:

	Control L	Control H	Sample 1	Sample 2	Sample 3
Mean (mmol/L)	1.98	3.00	0.93	2.56	4.24
Mean (mg/dL)	7.93	12.05	3.73	10.25	16.98
%CV					
Total	2.40	2.33	3.61	2.83	2.37
Between Day	1.61	1.86	2.57	2.26	1.99
Between Run	0.93	0.72	1.15	1.43	1.17

Creatinine:

To evaluate within run precision, ABX Pentra Urine Control L/H (level 1 & 2) and four human urine specimens were tested 20 times in a single run for each sample, per the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745). The results found were as follows:

	Control		Sample			
	Low	**High**	**1**	**2**	**3**	**4**
Mean (µmol/L)	4302	9249	984	8062	19767	25073
Mean (mg/dL)	48.6	104.5	11.1	91.1	223.4	283.3
%CV	2.09	1.34	4.44	1.73	1.51	1.88

To evaluate between run and total precision, ABX Pentra Urine Control L/H (level 1 & 2) and three human urine specimens were tested in 6 runs (one run per day, one calibration per run). The results found were as follows:

	Control L	Control H	Sample 1	Sample 2	Sample 3
Mean (µmol/L)	5489.25	12211.58	999.15	8390.83	18757.37
Mean (mg/dL)	62.03	137.99	11.29	94.82	211.96
%CV					

Total	1.23	4.04	4.60	2.30	3.25
Day to Day	0.33	3.90	2.20	1.29	3.08
Within Run	1.18	1.06	4.04	1.90	1.04

Phosphorus:

To evaluate within run precision, ABX Pentra Urine Control L/H (level 1 & 2) and five human urine specimens were tested 20 times in a single run for each sample, per the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745). The results found were as follows:

	Control		**Sample**				
	Low	**High**	**1**	**2**	**3**	**4**	**5**
Mean (mmol/L)	6.1	14.3	2.1	12.8	19.6	47.0	53.4
Mean (mg/dL)	19.0	44.2	6.6	39.8	60.9	145.6	165.4
%CV	1.67	0.80	3.87	1.21	0.94	1.78	0.79

To evaluate between run and total precision, ABX Pentra Urine Control L/H (level 1 & 2) and two human urine specimens were tested in duplicate for 20 days, two series per day, per the CLSI document, EP5-A. The results found were as follows:

	Control L	**Control H**	**Sample 1**	**Sample 2**
Mean (mmol/L)	6.3	14.8	2.3	29.8
Mean (mg/dL)	19.5	45.9	7.1	92.4
		%CV		
Total	2.82	2.06	5.95	1.97
Between Day	1.53	1.76	3.74	1.62
Between Run	1.89	0.75	1.44	0.95

b. Linearity/assay reportable range:

Amylase:

To evaluate linearity, different levels of amylase (from saliva) solutions were tested without post-dilution, in accordance with CLSI document, EP6-A. The acceptable bias with the linearity is ± 8%. Two studies were conducted, and the method was demonstrated to be linear from 105 to 2184 U/L and from 7.2 to 149.9 U/L. Combining the ranges, the data supports the linearity claim of 7.2 to 2000 U/L.

A study was performed to compare manual dilution with the automatic dilution performed by the Pentra 400. Human urines spiked with amylase solutions at different activities higher than the linearity were used, and the mean of manual and automatic results were calculated. The acceptable bias with the linearity is ± 8%. The samples ranged from 2166.4 to 5909.0 U/L and yielded acceptable bias,

substantiating the post-dilution claim of up to 6000 U/L.

Calcium:

To evaluate linearity, different concentrations of aqueous calcium solutions were tested without post-dilution, in accordance with CLSI document, EP6-A. The acceptable bias with the linearity is ± 10%. The method was demonstrated to be linear from 0.55 to 6.91 mmol/L (2.21 to 27.70 mg/dL), supporting the linearity claim of up to 6 mmol/L (24.06 mg/dL).

A study was performed to compare manual dilution with the automatic dilution performed by the Pentra 400. Human urines spiked with calcium solutions at different activities higher than the linearity were used, and the mean of manual and automatic results were calculated. The acceptable bias with the linearity is ± 10%. The samples ranged from 24.29 to 47.68 mg/dL and yielded acceptable bias, substantiating the post-dilution claim of up to 48.12 mg/dL.

Creatinine:

To evaluate linearity, different concentrations of aqueous creatinine solutions were tested without post-dilution, in accordance with CLSI document, EP6-A. The acceptable bias with the linearity is ± 8%. The method was demonstrated to be linear from 138 to 29070 µmol/L (1.56 to 328.49 mg/dL), supporting the linearity claim of up to 28000 µmol/L (316.4 mg/dL).

A study was performed to compare manual dilution with the automatic dilution performed by the Pentra 400. Human urines spiked with creatinine solutions at different activities higher than the linearity were used, and the mean of manual and automatic results were calculated. The acceptable bias with the linearity is ± 8%. The samples ranged from 29604 to 81372 µmol/L and yielded acceptable bias, substantiating the post-dilution claim of up to 84000 µmol/L (949.2 mg/dL).

Phosphorus:

To evaluate linearity, different concentrations of aqueous phosphate solutions were tested without post-dilution, in accordance with CLSI document, EP6-A. The acceptable bias with the linearity is ± 8%. The method was demonstrated to be linear from 1.72 to 67.69 mmol/L (5.33 to 209.84 mg/dL), supporting the linearity claim of up to 64 mmol/L (198.4 mg/dL).

A study was performed to compare manual dilution with the automatic dilution performed by the Pentra 400. Human urines spiked with phosphate solutions at different activities higher than the linearity were used, and the mean of manual and automatic results were calculated. The acceptable bias with the linearity is ± 8%. The samples ranged from 66.21 to 125.7 mmol/L and yielded acceptable bias, substantiating the post-dilution claim of up to 128 mmol/L (396.8 mg/dL).

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

The controls are biological source material. The serum from each donor contributing urine for this product was tested by FDA accepted methods and found non-reactive for Hepatitis B Surface Antigen (HBsAg), antibody to Hepatitis C (HCV) and antibody to HIV-1/HIV-2.

The values of the controls are assigned from the ABX PENTRA master calibrator, reagents and analyzers and are lot-specific. The target values are the median of multiple determinations. The values are verified by performing additional measurements and comparing the means to the values and conference ranges assigned.

The shelf-life stability of the controls was evaluated using two lots and was determined to be 2 years in unopened vials stored at 2-8°C. The stability after opening was evaluated by testing recovery of results between time of opening and time at expiration point. The stability was determined to be 30 days at 2-8°C, with vial tightly closed when not in-use.

d. Detection limit:

The minimum detection limit (MDL), based on the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745), is calculated from 30 measurements of physiological water (NaCl 0.9 g/L). The MDL is equal to the mean of the measurements + 4.65 SD.

Amylase: The MDL is 4.92 U/L.
Calcium: The MDL is 0.03 mmol/L or 0.12 mg/dL.
Creatinine: The MDL is 110.83 µmol/L or 1.3 mg/dL.
Phosphorus: The MDL is 0.41 mmol/L or 1.28 mg/dL.

e. Analytical specificity:

Interfering substances in solution were added to pooled human urine with two different analyte concentrations (normal and high), for each of the four analytes below. The interference study was performed following the Valtec guideline (Vassault et *al.*, Ann. Biol. Clin., 1986 (44), 686-745).

Amylase: Hemoglobin up to 290 µmol/L (500 mg/dL) and conjugated bilirubin up to 650 µmol/L (38 mg/dL) do not interfere with amylase determination by this test.

Calcium: Hemoglobin up to 278 µmol/L (479 mg/dL) and conjugated bilirubin up to 350 µmol/L (20.5 mg/dL) do not interfere with calcium determination by this test.

Creatinine: Hemoglobin up to 290 µmol/L (500 mg/dL) and conjugated bilirubin up to 650 µmol/L (38 mg/dL) do not interfere with creatinine determination by this test.

Phosphorus: Hemoglobin up to 213 µmol/L (367 mg/dL) and conjugated bilirubin up to 650 µmol/L (38 mg/dL) do not interfere with phosphorus determination by this test.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Comparison studies were performed using recommendations in CLSI EP9-A2.

Amylase:

One hundred and twenty-one (121) human urine specimens were analyzed on the subject device and a commercially available assay. The samples ranged from 13.3 to 1955.6 U/L. The linear regression equation was as follows: y = 1.133x + 42.179, r = 0.9945. Using Passing-Bablock regression procedure, y = 1.17x + 21.90, r = 0.9891. Based on CLSI EP21-A and the comparison study, the average bias is 9.1%.

Calcium:

One hundred and twenty-four (124) human urine specimens were analyzed on the subject device and a commercially available assay. The samples ranged from 0.26 to 23.68 mg/dL (0.06 to 5.90 mmol/L). The linear regression equation was as follows: y = 1.152x – 0.830, r = 0.9952. Using Passing-Bablock regression procedure, y = 1.13x – 0.50, r = 0.99. Based on the CLSI document EP21-A and the comparison study, the average bias is 1.0%.

Creatinine:

One hundred and ten (110) human urine specimens were analyzed on the subject device and a commercially available assay. The samples ranged from 2.8 to 311.5 mg/dL (248 to 27566 µmol/L). The linear regression equation was as follows: y = 0.977x + 1.152, r = 0.9976. Using Passing-Bablock regression procedure, y = 0.99x – 0.98, r = 0.9953. Based on the CLSI document EP21-A and the comparison study, the average bias is -1.1%.

Phosphorus:

One hundred and nineteen (119) human urine specimens were analyzed on the subject device and a commercially available assay. The samples ranged from 2.2 to 196.8 mg/dL (0.7 to 63.5 mmol/L). The linear regression equation was as follows: y = 1.091x – 2.555, r = 0.9946. Using Passing-Bablock regression procedure, y = 1.07x –

1.10, r = 0.9892. Based on the CLSI document EP21-A and the comparison study, the average bias is 2.4%.

b. Matrix comparison:

Not applicable

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 are provided in the package insert with the citation for the literature source.

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.