

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

A. 510(k) Number:

k060434

B. Purpose for Submission:

Notification of intent to manufacture and market new device

C. Measurand:

Albumin, micro albumin and total protein

D. Type of Test:

Quantitative

E. Applicant:

Horiba ABX

F. Proprietary and Established Names:

ABX PENTRA Albumin CP

ABX PENTRA Total Protein CP

ABX PENTRA Micro-albumin CP

ABX PENTRA μ -Alb Control L/H

ABX PENTRA μ -Alb Cal

ABX PENTRA N Control

ABX PENTRA P Control

ABX PENTRA Multical

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1035, Albumin test system

21 CFR 862.1635, Total protein test system

21 CFR 866.5040, Albumin immunological test system

21 CFR 862.1150, Calibrator

21 CFR 862.1660, Quality control material (assayed and unassayed)

2. Classification:

Class II (Albumin)

Class II (Total protein test system)

Class I (Microalbumin) - meets limitations of exemptions 21 862.9(c)(5)

Class II (Calibrator)

Class I (Controls), reserved

3. Product code:

CIX, Albumin test system

CEK, Total protein test system
DCF, Microalbumin
JIX, Calibrator, Multi-analyte
JIT, Secondary Calibrator
JJY, Quality control material (assayed and unassayed)

4. Panel:
Clinical Chemistry (75), Immunology (82)

H. Intended Use:

1. Intended use(s):

Proteins 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 Albumin CP reagent with associated calibrators and controls, is a diagnostic reagent for quantitative determination of Albumin in serum and plasma by colorimetry. Albumin measurements are used in the diagnosis and treatment of numerous diseases involving primarily the liver or kidneys.

ABX PENTRA Total Protein CP reagent with associated calibrators and controls, is a diagnostic reagent for quantitative 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.

ABX PENTRA Micro-albumin CP reagent with associated calibrators and controls, is a diagnostic reagent for quantitative in-vitro determination of Albumin in urine (μ ALB) at low concentrations by immunoturbidimetric assay. Measurements of albumin aids in the diagnosis of diabetic nephritis and other kidney and intestinal diseases.

The ABX PENTRA μ -Alb Cal is a calibrator for use in the calibration of quantitative Horiba ABX PENTRA Micro-albumin CP method on Horiba ABX clinical chemistry analyzers.

The ABX PENTRA μ -Alb Control L/H is for use in quality control by monitoring accuracy and precision for the quantitative ABX PENTRA Micro-albumin CP method.

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 P Control is for use in quality control by monitoring accuracy and precision.

2. Indication(s) for use:
See Intended Use above.
3. Special conditions for use statement(s):
For prescription use only
4. Special instrument requirements:
ABX PENTRA 400

I. Device Description:

The ABX PENTRA Albumin CP is an in vitro diagnostic assay for the quantitative determination of albumin in human serum and plasma based on a colorimetric test using Bromocresol Green (BCG). It is composed of a 99 mL mono-reagent cassette.

The ABX PENTRA Total Protein CP is an in vitro diagnostic assay for the quantitative determination of total proteins in human serum and plasma based on a colorimetric test (Biuret reaction). It is composed of a 61 mL mono-reagent cassette.

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 package insert (PI), providing optimal calibration of the appropriate HORIBA ABX 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 PI, providing control of the appropriate HORIBA ABX methods on the ABX PENTRA 400 analyzer. Each control is provided in ten vials of 5 mL.

The ABX PENTRA Micro-albumin CP is an in vitro diagnostic assay for the quantitative determination of albumin in human urine based on an immunoturbidimetric test. It is composed of a bi-reagent cassette, with 19 mL and 4.5 mL compartments.

The ABX PENTRA μ -Alb Cal is a liquid calibrator prepared by adding purified human albumin to a chemical buffer solution. It has 5 levels to be used for the calibration of the urinary albumin assay. The assigned values are given on the calibrator vials. This calibrator is provided in five vials of 1 mL.

The ABX PENTRA μ -Alb Control L/H is a liquid assayed control prepared by adding

purified human albumin to a chemical buffer solution. It has 2 levels (Low and High) to be used for the quality control of the urinary albumin assay. The assigned values are given in the PI. Each level of this calibrator is provided in two vials of 1 mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):
PSI Albumin Reagent Set, Raichem Spia Microalbumin Reagent, Raichem Spia Microalbumin Control Set, Cobas Ready Total Protein Reagent
2. Predicate 510(k) number(s):
k822471, k903123, k891475, k896230
3. Comparison with predicate:

	Predicate device (k822471):	Device :
Device Name	Albumin Reagent Set	ABX Pentra Albumin CP
Analytes	Albumin	Albumin
Method :	Colorimetric determination using Bromcresol Green	Colorimetric determination using Bromcresol Green
Specimen :	Serum	Serum & Plasma
Component reagent matrices	Single-reagent bottle, ready to use: REAGENT : Bromcresol Green, buffer, surfactant, non-reactive ingredients, stabilizers	Mono-reagent cassette, ready to use: REAGENT : Succinate buffer, Bromcresol Green, Brij 35
Format	Liquid	Liquid
Labels	-	Horiba ABX specific label
Packaging	Single-reagent bottle REAGENT : 1 x 120 ml	Mono-reagent cassette : REAGENT : 99 ml
Performance data :		
Number of tests	-	327 tests
Sample volume	2 µl/test	2 µl/test
Detection limit	-	0.02 g/dL
Accuracy and Precision	CV Total <4.2%	CV Total < 1.86%
Measuring range	Up to 6 g/dL	0.46 g/dL – 5.60 g/dL
Upper linearity limit	6 g/dL, and with automatic post-dilution 12 g/dL)	5.60 g/dL, and with automatic post-dilution 11.20 g/dL)
Calibration stability	N/A	14 days
Closed reagent stability	Until the expiration date when stored at room temperature	36 months at 2-8°C
Open Reagent stability	Until the expiration date when stored at room temperature	on-board stability (refrigerated area): 83 days

	Predicate device (k903123):	Device :
Device Name	Microalbumin Reagent	ABX Pentra Micro-albumin CP
Analytes	Albumin	Albumin
Method :	Immunoturbidimetric assay	Immunoturbidimetric assay
Specimen :	Urine	Urine
Component reagent matrices	Single reagent bottles, ready to use: MICROALBUMIN ANTIBODY REAGENT : anti-human albumin antibody (goat), buffers, stabilizers, preservatives POLYMER BUFFER : enhancers, buffers, stabilizers, preservatives SAMPLE DILUENT : buffers and preservatives	Bi-reagent cassette, ready to use REAGENT 1 : Glycine buffer solution REAGENT 2 : Anti-human albumin antibody (goat)
Format	Liquid	Liquid
Packaging	Kit composed of single-reagent bottles MICROALBUMIN ANTIBODY REAGENT : 2 x 3 ml POLYMER BUFFER : 1 x 120 ml SAMPLE DILUENT : 2 x 25 mL	Bi-reagent cassette : REAGENT 1 : 19 mL REAGENT 2 : 4.5 mL
Performance data :		
Number of tests	-	150 tests
Sample volume	50 µl/test	12 µl/test
Detection limit	6 mg/L	4 mg/L
Accuracy and Precision	CV Total < 2.3%	CV Total < 7.99%
Measuring range	Up to 218 mg/L	9.0 mg/L – 200.0 mg/L
Upper linearity limit	218 mg/L	200 mg/L, and with automatic post-dilution 2000 mg/L
Calibration stability	N/A	7 days
Closed reagent stability	Until the expiration date when stored at 2-8°C	24 months at 2-10°C
Open Reagent stability	Until the expiration date when stored at 2-8°C	on-board stability (refrigerated area): 23 days

	Predicate device (k896230):	Device :
Device Name	Total Protein	ABX Pentra Total Protein CP
Analytes	Total Protein	Total Protein
Method :	Colorimetric determination using the Biuret reaction	Colorimetric determination using the Biuret reaction
Specimen :	Serum Plasma	Serum Plasma
Component reagent matrices	Single-reagent bottles, ready to use: REAGENT 1 : sodium hydroxide, buffers, stabilizers, fillers REAGENT 2 : sodium hydroxide, sodium potassium tartrate, potassium iodide, cupric sulfate, buffers, stabilizers, fillers	Mono-reagent cassette, ready to use: REAGENT : Potassium iodide, potassium sodium tartrate, copper sulfate, sodium hydroxide
Format	Liquid	Liquid
Packaging	Single-reagent bottles REAGENT 1 : 3 x 100 ml REAGENT 2 : 1 x 100 ml	Mono-reagent cassette : REAGENT : 61 ml
Performance data :		
Number of tests	-	300 tests
Sample volume	5 µL/test	2 µl/test
Detection limit	-	0.14 g/dL
Quantification limit		0.60 g/dL
Accuracy and Precision	CV Total < 2.4%	CV Total < 2.82%
Measuring range	Up to 12 g/dL	0.60 g/dL – 10.00 g/dL
Upper linearity limit	12 g/dL, and with automatic post-dilution 15 g/dL	10 g/dL, and with automatic post-dilution 20 g/dL
Calibration stability	Calibration required monthly	1 day
Closed reagent stability	Until the expiration date when stored at 15-25°C	36 months at 2-8°C
Open Reagent stability	Until the expiration date when stored at 15-25°C	on-board stability (refrigerated area): 6 days

	Predicate device (k903123):	Device :
Device Name	Microalbumin Calibrator Set (included in the Microalbumin Reagent kit from Raichem)	ABX Pentra μ -Alb Cal
Method :	Calibration of Raichem albumin measurement method in urine	Calibration of HORIBA ABX albumin in urine
Component matrices	Vials (liquid) 5 levels Human serum based with added preservatives and stabilizers	Vials (liquid) 5 levels: 12.5, 25, 50, 100 and 200 mg/L Purified human albumin added to a chemical buffer solution
<i>Calibrated molecules</i>	Albumin	Albumin : the calibrator values are given on the vial labels
Format	Liquid, ready to use	Liquid, ready to use
Packaging	Kit composed of : 5 x 1 mL vial	Kit composed of : 5 x 1 mL vial
Performance data :		
Calibration value	- Established using the Raichem Microalbumin Reagents and the College of American Pathologists Reference Preparation for Proteins in Human Serum (RPPHS) - The concentration of each calibrator is listed on the vial label	- Determined using the method of molecular extinction coefficient of human sera albumin - The concentration of each calibrator is given on the vial label
Closed stability	Up to the expiration date at 2-8°C	12 months at 2-10°C
Open stability	Up to the expiration date at 2-8°C	4 weeks at 2-10°C 3 months at -20°C

	Predicate device (k891475):	Device :
Device Name	Microalbumin Control Set (included in the Microalbumin Reagent kit from Raichem)	ABX Pentra μ -Alb Control L/H
Method :	Single-parameter control by monitoring the performances of albumin determination in urine with Microalbumin Reagent	Single-parameter control by monitoring the performances of albumin determination in urine with ABX Pentra Micro-albumin CP reagent

	Predicate device (k891475):	Device :
Device Name	Microalbumin Control Set (included in the Microalbumin Reagent kit from Raichem)	ABX Pentra μ -Alb Control L/H
Component reagent matrices	Vial (liquid) 2 levels Human serum based, buffers, stabilizers and fillers	Vial (liquid) 2 levels : Low / High Purified human albumin added to a chemical buffer solution
Controlled molecules	Albumin : the exact control values are given in the notice	Albumin : the exact control values are given in the PI
Format	Liquid	Liquid, ready to use
Packaging	Level 1 : 1 x 1 mL Level 2 : 1 x 1 mL	Kit composed of : 2 x 1 mL Low Control 2 x 1 mL High Control
Performance data : Theoretical values and confidence intervals	<ul style="list-style-type: none"> - The assay values and range listed are established using the Raichem SPIA Microalbumin Reagents and Calibrators traceable to international reference material, CRP 470. - The values are lot specific - The assay values and ranges are listed in the notice enclosed in the kit 	<ul style="list-style-type: none"> - The assigned values are determined by calculating the mean value obtained from multiple determinations. - The assigned values for both Low and High controls are lot specific - The assigned values and precise confidence interval are indicated in the annex enclosed in the kit
Closed stability	Up to the expiration date at 2-8°C	12 months at 2-10°C
Open stability	Up to the expiration date at 2-8°C	4 weeks at 2-10°C

	Device (k052007):	Device :
Device Name	ABX Pentra Multical	ABX Pentra Multical
Performance data :		Unchanged
Calibration values	<ul style="list-style-type: none"> - Determined using parameter-specific methods (mentioned in the annex) under strictly standardized conditions on Horiba ABX analyzers using Horiba ABX system reagents and Horiba ABX master calibrator - The calibration value specified is the median of the values obtained - The assigned values are indicated in the annex enclosed in the kit. 	Unchanged

	Device (k052007):	Device :
Device Name	ABX Pentra Multical	ABX Pentra Multical
Closed stability	- The values are lot-specific. 24 months at 2-8°C	Unchanged
Component** stability after reconstitution of the calibrator	At 15 to 25°C : 8 hours At 2 to 8°C : 2 days At -25°C to -15°C : 2 weeks (when frozen once) **Exceptions: Stability of Direct Bilirubin At 15 to 25°C : 3 hours At 2 to 8°C : 8 hours At -25°C to -15°C : 2 weeks (when frozen once) Stability of Total Bilirubin At 15 to 25°C : 6 hours At 2 to 8°C : 1 day At -25°C to -15°C : 2 weeks (when frozen once)	Unchanged
Additional Components		Addition of Albumin and Total Protein

	Predicate device (k052007):	Device :
Device Name	ABX Pentra N and P Controls	ABX Pentra N and P Controls
Packaging	Kit composed of : 10 x bottle, each with lyophilizate for 5 mL control	Unchanged
Performance data :		
Theoretical values and confidence intervals	- The theoretical value specified is the median of the values obtained, the confidence interval equals the theoretical value \pm 3SD (SD = Standard Deviation) - The assigned values are indicated in the annex enclosed in the kit. - The values are lot-specific.	Unchanged
Closed stability	30 months at 2-8°C	Unchanged
Components** stability after reconstitution of the calibrator	At 15 - 25°C : 12 hours At 2 - 8°C : 5 days At (-15°C) - (-25°C) : 1 month (when frozen once) **Exceptions: Stability of Total Bilirubin	Unchanged

	Predicate device (k052007):	Device :
Device Name	ABX Pentra N and P Controls	ABX Pentra N and P Controls
	At 15 - 25°C : 8 hours At 2 - 8°C : 24 hours At (-15°C) - (-25°C) : 2 weeks (when frozen once) Stability of Direct Bilirubin At 15 - 25°C : 4 hours At 2 - 8°C : 8 hours At (-15°C) - (-25°C) : 2 weeks (when frozen once)	
Additional Components		Addition of Albumin and Total Protein

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

- 1) Valtec guideline: Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745).
- 2) CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods.
- 3) CLSI EP6-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach.
- 4) CLSI EP9-A2, Method Comparison and Bias Estimation Using Patient Samples.
- 5) CLSI EP17-A, Protocols for Determination of Limits of Detection and Limits of Quantitation.

L. Test Principle:

For albumin, a colorimetric test is used using Bromocresol Green dye-binding procedure. At pH 4.20, in succinate buffer and with a nonionic surfactant Brij35, the Bromocresol Green (BCG) fixes itself selectively to the albumin of the sample, producing a blue color which is measured at 628 nm. The intensity of the coloring is directly proportional to the albumin concentration.

For micro-albumin, anti-albumin antibodies of the reagent react with albumin of the sample by forming antigen-antibody complexes. The resulting agglutination is measured by turbidimetry. The obtained absorbance change is proportional to the quantity of microalbumin in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from calibrators of known concentration.

For total protein, the protein, in an alkaline solution and in the presence of copper ions, form a purple colored complex between the Biuret (NH₂-CO-NH-CO-NH₂) and two consecutive peptidic connections. The resulting complex's color is directly proportional to the protein concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. *Precision/Reproducibility:*

Within Run:

For the Albumin CP reagent, within-run precision was determined using 2 controls (ABX PENTRA N and P Controls) and 3 serum specimens of low, medium and high concentrations were tested 20 times in a single run for each sample (in accordance with the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745). Results are described below.

In g/dL	N Control	P Control	Sample 1	Sample 2	Sample 3
Mean	3.39	3.34	2.30	4.15	5.60
SD	0.02	0.03	0.01	0.02	0.05
%CV	0.59	0.84	0.44	0.47	0.83

For the Micro-albumin reagent, within-run precision was determined using 2 controls (ABX Pentra μ -Alb Control L/H) and 3 urine specimens of low, medium and high concentrations tested 20 times in a single run for each sample (in accordance with the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745). Results are described below.

In mg/L	L Control	H Control	Sample 1	Sample 2	Sample 3
Mean	24.74	101.37	13.68	79.99	166.08
SD	0.65	0.71	0.72	0.47	1.32
%CV	2.61	0.70	5.27	0.58	0.79

For the Total Protein reagent, within-run precision was determined using 2 controls (ABX PENTRA N and P Controls) and 3 serum specimens of low, medium and high concentrations tested 20 times in a single run for each sample (in accordance with the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745). Results are described below.

In g/dL	N Control	P Control	Sample 1	Sample 2	Sample 3
Mean	5.16	5.17	4.23	6.06	7.93
SD	0.1	0.1	0.1	0.1	0.1
%CV	1.01	1.24	1.12	0.87	0.69

Between Run:

For the Albumin CP reagent, between-run precision NCCLS (CLSI) EP-5A was followed using two serum specimens of low & high levels and 2 controls tested in duplicate for 20 days, two series per day (for a total of 80). Results are described below.

In g/dL		N Control	P Control	Sample 1	Sample 2
	Mean	3.40	3.31	2.35	4.25
Between Run	SD	0.04	0.03	0.03	0.07
	%CV	1.06	0.85	1.49	1.74
Total	SD	0.04	0.03	0.04	0.08
	%CV	1.27	0.98	1.67	1.86

For the Micro-albumin reagent, between-run precision NCCLS (CLSI) EP-5A was followed using two urine specimens of low & high levels and 2 controls tested in duplicate for 20 days, two series per day (for a total of 80). Results are described below.

In mg/L		L Control	H Control	Sample 1	Sample 2
	Mean	26.46	100.86	22.73	169.52
Between Run	SD	0.70	1.23	0	3.14
	%CV	2.64	1.22	0	1.85
Total	SD	1.21	2.08	1.82	4.09
	%CV	4.57	2.06	7.99	2.41

For the Total Protein CP reagent, between-run precision NCCLS (CLSI) EP-5A was followed using two serum specimens of low & high levels and 2 controls tested in duplicate for 20 days, two series per day (for a total of 80). Results are described below.

In g/dL		N Control	P Control	Sample 1	Sample 2
	Mean	5.25	5.19	4.50	6.67
Between Run	SD	0.07	0.08	0.06	0.11
	%CV	1.39	1.46	1.38	1.59
Total	SD	0.13	0.12	0.13	0.15
	%CV	2.51	2.37	2.82	2.19

b. Linearity/assay reportable range:

Linearity for Albumin CP was assessed for non-post dilution samples in accordance with CLSI EP6-A. Samples used for this study were concentrated human sera using ultrafiltration. Ten different levels of albumin (each tested 4 times) were prepared based on the dilution of the highest concentration solution level with a solution near the low limit of detection resulting in a range of samples from 0.62 to 6.16 g/dL. The linearity of the albumin assay was evaluated by comparing observed versus expected values across the expected range. A linear regression analysis was performed on the data and plotted. The sponsor's acceptable bias for recovery of the samples is $\pm 8\%$. The observed linearity across the reportable range has a slope of 0.9335, and an intercept of 0.1252. The assay range was demonstrated to be linear from 0.62 to 6.16 g/dL. The sponsor will claim a range of 0.46 (the lowest value of the comparison study) to 5.60 g/dL. Recovery of post dilution serum samples was also assessed comparing manual versus automatic dilution by the PENTRA 400. Nine samples were each tested 4 times and ranged from 6.26 to 10.98 g/dL. The sponsor's acceptable bias for recovery of the samples is $\pm 8\%$. The data supports the sponsor's claim of a post dilution limit of 11.2 g/dL.

Linearity for Micro-albumin was assessed for non-post dilution samples in

accordance with CLSI EP6-A. Samples used for this study were human urine. Ten different levels of albumin (each tested 4 times) were prepared based on the dilution of the highest concentration solution level with a solution near the low limit of detection resulting in a range of samples from 16.6 to 195.6 mg/L. The linearity of the albumin assay was evaluated by comparing observed versus expected values across the expected range. A linear regression analysis was performed on the data and plotted. The sponsor's acceptable bias for recovery of the samples is $\pm 10\%$. The observed linearity across the reportable range has a slope of 0.9697, and an intercept of 5.8868. The assay range was demonstrated to be linear from 16.6 to 195.6 mg/L. The sponsor will claim a range of 9 (the lowest value of the comparison study) to 200 mg/L. Recovery of post dilution serum samples was also assessed comparing manual versus automatic dilution by the PENTRA 400. Eleven samples were each tested 4 times and ranged from 219.3 to 1904.8 mg/L. The sponsor's acceptable bias for recovery of the samples is $\pm 10\%$. The data supports the sponsor's claim of a post dilution limit of 2000 mg/L.

Linearity for Total Protein CP in serum was assessed in accordance with CLSI EP6-A. Samples used for this study were concentrated human sera using ultrafiltration. Eleven different levels of total protein (each tested 4 times) were prepared based on the dilution of the highest concentration solution level with a solution near the low limit of detection resulting in a range of samples from 0.675 to 12.02 g/dL. The linearity of the total protein assay was evaluated by comparing observed versus expected values across the expected range. A linear regression analysis was performed on the data and plotted. The sponsor's acceptable bias for recovery of the samples is $\pm 5\%$. The observed linearity across the reportable range has a slope of 0.9961, and an intercept of 0.1196. The assay range for serum was demonstrated to be linear from 0.7 to 12.0 g/dL. The sponsor will claim a range of 0.6 (the limit of quantitation) to 10.0 g/dL. Recovery of post dilution serum samples was also assessed comparing manual versus automatic dilution by the PENTRA 400. Eleven samples were each tested 4 times and ranged from 11.54 to 20.08 g/dL. The sponsor's acceptable bias for recovery of the samples is $\pm 4\%$. The data supports the sponsor's claim of a post dilution limit of 20 g/dL.

The sponsor demonstrated linearity of Total Protein CP results in Lithium Heparin plasma samples through a linearity study. Nine different levels of total protein (each tested 4 times) were prepared based on the dilution of the highest concentration solution level with a solution near the low limit of detection resulting in a range of samples from 2.339 to 11.867 g/dL. The linearity of the total protein assay was evaluated by comparing observed versus expected values across the expected range. A linear regression analysis was performed on the data and plotted. The sponsor's acceptable bias for recovery of the samples is $\pm 5\%$. The observed linearity across the reportable range has a slope of 1.0027, and an intercept of 0.094. The assay range for plasma was demonstrated to be linear from 2.3 to 11.8 g/dL. The sponsor will

claim a range of 0.6 (the limit of quantitation) to 10.0 g/dL for plasma samples.

- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Albumin CP reagent stability was tested in real-time with reagents stored at 2-8°C using 3 different lots. Real time stability was determined to be 36 months. On-board stability was determined to be 83 Days.

Micro-albumin CP reagent stability was tested in real-time with reagents stored at 2-8°C using 3 different lots. Real time stability was determined to be 24 months. On-board stability was determined to be 23 Days. For the Micro-albumin controls, stability studies determined a calibration time stability of 11 days allowing a claim of 7 days. After this period, urinary albumin method on ABX Pentra 400 using ABX Pentra Micro-Albumin CP reagent has to be re-calibrated.

Albumin CP reagent stability was tested in real-time with reagents stored at 2-8°C using 3 different lots. Real time stability was determined to be 36 months. On-board stability was determined to be 83 Days.

Total Protein CP reagent stability was tested in real-time with reagents stored at 2-8°C using 3 different lots. Real time stability was determined to be 36 months. On-board stability was determined to be 6 Days.

The ABX PENTRA μ -Alb Control L/H are the same product as the ABX PENTRA μ -Alb Cal level 25 and 100 mg/L. As such, the stability studies for the ABX PENTRA μ -Alb Control L/H are the same as the stability studies for the ABX PENTRA μ -Alb Cal. ABX Pentra μ -Alb Cal was determined through real time stability studies that the stability at 2 - 10°C is 12 months. ABX Pentra μ -Alb Cal was determined through real time stability studies that the open vial stability is 4 weeks between 2-10°C or 3 months at -20°C.

For ABX PENTRA N Control & ABX PENTRA P Control traceability, the values of the ABX PENTRA Controls are assigned from the ABX PENTRA calibrator, reagents and analyzers. The target value is determined by the median of results from 150 measurements/parameters. Confidence range is determined as the calculated range in percent which is based on the experimental results from the previous target value trials. The range declared in the target value sheet is equal to the assigned value +/- 3 standard deviations (3 SD).

For ABX Pentra Multical traceability, the ABX Pentra Multical is prepared from reference materials. Commercial calibrators are standardized by means of a master lot which is stored at -80°C. Two controls are used to ensure that the calibration values of the master lot, as well as the entire measurement system (calibrator, reagent, and analyzer), remain stable during the storage

period. The target value is determined by the median of results from 150 measurements/parameters.

For the ABX PENTRA N Control, ABX PENTRA P Control, and ABX PENTRA Multical, protocols and acceptance criteria for open and closed stability of the controls and calibrators were described and found to be acceptable.

d. Detection limit:

The detection limit for the Albumin CP was determined by measuring 30 measurements of saline water (NaCl 0.9 g/L) + 4.65 SD. The limit of detection for the Albumin CP assay was determined to be 0.02 g/dL.

Because the measurement of saline water is not possible with the normal application of the Micro-albumin assay (no results available when sample concentration is lower than the calibration curve), usual measurement of MDL (30 measurements of saline water) is not possible. For the specific proteins the Minimum Interpretation Limit (MIL) was used. Like MDL, MIL is the lower concentration that could be distinguished from 0, concentration calculated using the rate absorbency measurement of known concentration's samples and saline water. The limit of detection for the Micro-albumin CP assay was determined to be 4 mg/L.

For the Total Protein CP assay, the limit of the blank (LoB) was determined using physiological water (0.9% NaCl) assayed 90 times on 3 different PENTRA 400 instruments. The LoB was determined as the mean of results + 1.645*SD which was 0.05 g/dL. The limit of detection (LoD) was then determined with 4 samples with concentrations between LoB and LoB x 5 assayed 20 times and using $LoD = LoB + 1.645 * \text{standard deviation}$. To determine the limit of quantitation (LoQ), samples with concentrations of total protein above the lower limit of the linear range (0.70 g/dL for serum and 2.30 g/dL for protein) were run to determine precision and recovery. The samples, with a known concentration, were assayed 10 times. The sponsor's acceptance criteria is within-run precision being %CV <15% and bias <10%. Using these criteria, it was determined that the LoQ for plasma samples was 0.26 g/L and 0.58 g/L for serum samples. The sponsor will claim a LoQ of 0.60 g/dL for the total protein assay.

e. Analytical specificity:

For Albumin CP: In accordance with the Valtec guideline, the tested interferants were added to the base pooled serum at two different albumin concentrations (normal and high). The base serum with each substance was then serially diluted with the same base serum that was added saline instead of substance to adjust albumin concentration. Hemoglobin up to 232 µmol/L (400 mg/dL), total bilirubin up to 616 µmol/L (36 mg/dL), direct bilirubin up to 616 µmol/L (36 mg/dL), and triglycerides (as Intralipid ®, representative of

lipemia, up to 7 mmol/L (612.5 mg/dL) do not show significant interference with albumin determination. The sponsor also described through references that some globulins could give an “albumin like coloration,” however states that the procedure used on Pentra 400 eliminates this type of interference by a fast reading. The sponsor states in the labeling that Ampicillin has been found to seriously interfere with this type of colorimetric method.

For Micro-albumin CP: Substances were added to the base urine at two different albumin concentrations (normal and high). The base urine with each substance was then serially diluted with the same base urine that was added saline instead of substance to adjust albumin concentration. Hemoglobin up to 260 µmol/L (450 mg/dL), Ascorbic acid up to 5 g/L, Total Bilirubin up to 20 mg/dL, Urobilin up to 10 mg/dL, Creatinine up to 240 mg/dL do not show significant interference with urinary albumin determination. The sponsor also determined a prozone effect for the Micro-albumin assay to occur at 1200 mg/L with dilution being effective in overcoming the effect.

For Total Protein CP: In accordance with the Valtec guideline, the tested interferants were added to the base pooled serum at two different total protein concentrations (normal and high). The base serum with each substance was then serially diluted with the same base serum that was added saline instead of substance to adjust total protein concentration. Hemoglobin up to 72.5 µmol/L (1.25 g/L), total bilirubin up to 616 µmol/L (36 mg/dl), direct bilirubin up to 616 µmol/L (36 mg/dl) and triglycerides (as Intralipid) up to 4.6 mmol/L (355 mg/dl) do not show significant interference with total proteins determination by this test. The sponsor also described through references that some globulins could give an “albumin like coloration,” however states that the procedure used on Pentra 400 eliminates this type of interference by a fast reading. The sponsor states in the labeling that Ampicillin has been found to seriously interfere with this type of colorimetric method.

f. Assay cut-off:
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

A total of 136 serum samples were assayed using the Albumin CP reagents on the PENTRA 400 and a commercially available method. Samples ranged from 0.46 to 5.40 g/dL. Diluted samples (43) were used to cover the range of the assay. Linear regression analysis gave the following relationship: $\text{Device} = 0.943(\text{Predicate}) + 0.042$; $r = 0.9944$.

A total of 126 urine samples were assayed using the Micro-albumin CP reagents on the PENTRA 400 and a commercially available method. Samples ranged from 9.0 to 198.0 mg/L. Spiked samples (96) were used to cover the

range of the assay. Linear regression analysis gave the following relationship:
 $\text{Device} = 0.899(\text{Predicate}) + 5.003$; $r = 0.9964$.

A total of 115 serum samples were assayed using the Total Protein CP reagents on the PENTRA 400 and a commercially available method. Samples ranged from 0.73 to 9.66 g/dL. Diluted samples (17) were used to cover the range of the assay. Linear regression analysis gave the following relationship:
 $\text{Device} = 1.0255(\text{Predicate}) + 0.0507$; $r^2 = 0.9841$.

A total of 262 lithium heparin plasma samples were assayed using the Total Protein CP reagents on the PENTRA 400 and a commercially available method. Samples ranged from 0.70 to 10.24 g/dL. Diluted or spiked samples (21) were used to cover the range of the assay. Linear regression analysis gave the following relationship: $\text{Device} = 1.013(\text{Predicate}) + 0.098$; $r = 0.9922$.

b. Matrix comparison:

The sponsor demonstrated equivalence of Albumin CP results in serum and Lithium Heparin plasma samples by using 74 clinical samples (29 spiked or diluted) spanning a range of 2.16 to 5.48 g/dL. Linear regression showed a slope of 0.9961 and an intercept of -0.013, and a correlation coefficient of 0.998.

The sponsor demonstrated equivalence of Total Protein CP results in serum and Lithium Heparin plasma samples by using 37 clinical samples spanning a range of 0.70 to 10.24 g/dL. The mean relative bias was found to be 5%.

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:

In the labeling the sponsor makes the recommendation that each laboratory establish its own reference ranges for each of these analytes.

The values provided for Albumin in labeling as a guideline are based upon the literature as follows:

Age:	g/dL
0 - 4 days:	2.8-4.4
4 days – 14 years:	3.8-5.4
14 – 18 years:	3.2-4.5
Adults (20 – 60 years):	3.5-5.2
60 – 90 years:	3.2-4.6
> 90 years:	2.9-4.5

Roberts W.L., McMillin G.A., Burtis C.A., Bruns, D.E., Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4th Ed., Burtis C.A., Ashwood E.R., Bruns, D.E., (Elsevier Saunders eds., St. Louis, USA), (2006), 2254.

The values provided in the labeling for Micro-albumin is <25 mg/L based on an internal patient study using 214 fresh urine samples using a confidence interval of 95% on the distribution of the results.

The values provided in the labeling for Total Protein are based upon literature¹ as follows:

Ambulatory patients :	Recumbent patients :
64 - 83 g/L	60 - 78 g/L
6.4 - 8.3 g/dL	6.0 - 7.8 g/dL

The following statement based upon literature² is also included in the labeling. “Serum and plasma can be used for total protein determination. Due to fibrinogen, the mean total protein concentration in plasma is higher than in serum, i.e. specifically by +.25 g/dL in blood donors, by +.36 g/dL in nonhospitalized patients, by +.46 g/dL in hospitalized patients and by +.66 g/dL in hospitalized patients with a CRP <50mg/dL.”

References:

¹Roberts W.L., McMillin G.A., Burtis C.A., Bruns, D.E., Reference Information for the Clinical Laboratory, TIETZ Textbook of Clinical Chemistry and Molecular Diagnostics. 4^{ème} Ed., Burtis C.A., Ashwood E.R., Bruns, D.E., (Elsevier Saunders eds., St Louis, USA), (2006), 2293

²Thomas L. Clinical Laboratory Diagnostics. 1st ed. Frankfurt: TH-Books Verlagsgesellschaft; 1998. p. 644-647

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.