

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

A. 510(k) Number:

k061138

B. Purpose for Submission:

New Submission

C. Measurand:

C-Reactive Protein

D. Type of Test:

Quantitative immunoturbidimetric assay

E. Applicant:

Horiba ABX

F. Proprietary and Established Names:

ABX Pentra 400 : CRP CP

G. Regulatory Information:

1. Regulation section:

21CFR Sec.- 866.5270-C-reactive protein immunological test system.

21CFR Sec.- 862.1150 Calibrator.

21CFR Sec.- 862.1660 Quality control material (assayed and unassayed).

2. Classification:

II

3. Product code:

DCK - C-Reactive Protein, Antigen, Antiserum, And Control

JIS - Calibrator, Primary

JJX - Single (specified) analyte controls (assayed and unassayed)

JJY - Multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

Immunology (82), Chemistry (75)

H. Intended Use:

1. Intended use(s):

See Indication(s) for use below:

2. Indication(s) for use:

CRP reagent, with associated calibrators and controls, are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer to measure C-reactive Protein analyte.

The ABX PENTRA CRP Cal is a calibrator for use in the calibration of quantitative Horiba ABX PENTRA CRP CP method on Horiba ABX clinical chemistry analyzers.

The ABX PENTRA Low CRP Control is for use in quality control by monitoring accuracy and precision for the quantitative ABX PENTRA CRP CP method.

ABX PENTRA CRP CP reagent with associated calibrators and controls are for

quantitative in vitro diagnostic determination of the C-reactive protein in human serum and plasma based on an immunoturbidimetric assay.

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

Measurement of C-reactive protein aids in evaluation of the amount of injury to body tissue.

3. Special conditions for use statement(s):
The ABX PENTRA CRP reagent is for conventional CRP use only
For professional use
4. Special instrument requirements:
ABX PENTRA 400 Clinical Chemistry Analyzer

I. Device Description:

The ABX Pentra CRP CP assay is ready-to-use, composed of a bi-reagent cassette, with 25 ml and 23.5 ml compartments.

Reagent 1: Buffer solution:

Glycine buffer solution

Reagent 2: Latex suspension:

0.20 % w/v suspension of latex particles sensitized with anti-CRP antibodies (rabbit)

The ABX PENTRA CRP Cal is a liquid human serum calibrator with chemical additives. It has 5 levels to be used for the calibration of the CRP assay. The assigned values are given on the calibrator vials. This calibrator is provided in five vials of 1 ml.

The ABX PENTRA Immuno I Control L/H is a lyophilized two-level quality control product consisting of human serum. The assigned values of the control components are given in control annex ensuring control of the appropriate HORIBA ABX methods on the ABX PENTRA 400 analyzer. Each level of control is provided in one vial of 3 ml.

The ABX PENTRA Low CRP Control is a liquid assayed control prepared by diluting CRP at low concentration in human serum. It has to be used for the quality control of low levels measured with the CRP assay. The assigned value is given in the control annex. This control is provided in four vials of 1 ml.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Kamiya, K-Assay C-Reactive Protein, Kamiya, K-Assay hs-CRP Controls
2. Predicate 510(k) number(s):
k023828, k022486
3. Comparison with predicate:

	Predicate device (k023828):	Device :
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Device Name	K-ASSAY CRP (3)	ABX Pentra CRP CP
Method :	Latex-enhanced Immunoturbidimetric assay	Latex-enhanced Immunoturbidimetric assay
Specimen :	Serum Plasma	Serum Plasma
Component reagent matrices	Two reagent bottles: REAGENT 1: Buffer Reagent: Glycine buffer solution. REAGENT 2: Latex suspension: 0.20% (w/v) suspension of latex particles sensitized with anti- CRP antibodies (rabbit).	Bi-reagent cassette, ready to use: REAGENT 1 : Buffer solution: Glycine buffer solution. REAGENT 2 : Latex suspension: 0.20% (w/v) suspension of latex particles sensitized with anti- CRP antibodies (rabbit).
Format	Liquid	Liquid
Packaging	Two reagent bottles: REAGENT 1: 1 x 50 ml REAGENT 2: 1 x 50 ml	Bi-reagent cassette : REAGENT 1 : 25 ml REAGENT 2 : 23.5 ml
Performance data :		
Sample volume	On Hitachi 917: 3 µl/test	4 µl/test
Detection limit	Standard sensitivity: 0.1 mg/l High sensitivity: 0.05 mg/l Wide sensitivity : 0.2 mg/l	0.09 mg/l determined according to the CLSI (NCCLS), EP- 17A protocol
Accuracy and Precision	CV Total < 6.97%	CV Total < 7.04%
Assay Linearity	Standard sensitivity: 0.1 mg/l - 320 mg/l High sensitivity: 0.05 mg/l – 160 mg/l Wide sensitivity : 0.2 mg/l – 480 mg/l	Up to 160 mg/l

ABX Pentra CRP Cal:

	Predicate Device (k023828):	Device :
Device Name	K-ASSAY CRP Calibrator Set E	ABX Pentra CRP Cal
Method :	Calibration of K-ASSAY CRP (3) on clinical chemistry analyzers	Calibration of ABX Pentra CRP CP on clinical chemistry analyzers
Component matrices	Vial (liquid) Human serum with chemical (preservative) and biological additives	Vial (liquid) Human serum with chemical (preservative) and biological additives
Format	Liquid, ready-to-use	Liquid, ready-to-use
Packaging	Kit composed of : 5 x 2 ml vial	Kit composed of : 5 x 1 ml vial
Calibration values	- Traceable to IFCC CRM470.	- Determined using primary calibration with CRM n°470-CAP/IFCC, lot. 91/06- 19.

ABX Pentra Immuno I Control L/H:

	Predicate device (k022486):	Device :
Device Name	K-ASSAY hs-CRP Control Set	ABX Pentra Immuno I Control L/H
Method :	Single parameter control by monitoring the performance of C-Reactive Protein immunoturbidimetric assays.	Quality control by monitoring accuracy and precision for the quantitative methods as specified in the enclosed value sheet.
Component matrices	Vials (liquid) 2 levels Pool of Human sera with chemical additives (preservatives)	Vials (lyophilizate) 2 levels Pool of Human sera with chemical additives (preservatives)
Format	Liquid, ready-to-use	Lyophilizate (to reconstitute with distilled/deionised water – not provided)
Packaging	Kit composed of : Level 1: 2 x 1 ml vial (blue cap) Level 2: 2 x 1 ml vial (red cap)	Kit composed of : 2 x bottle, each with lyophilizate for 3 ml control.

ABX Pentra Low CRP Control:

	Predicate device (k022486):	Device :
Device Name	K-ASSAY hs-CRP Control Set	ABX Pentra Low CRP Control
Method :	Single parameter control by monitoring the performance of C-Reactive Protein immunoturbidimetric assays.	Single parameter control by monitoring the performances of C-Reactive Protein determination at low concentration.
Component matrices	Vials (liquid) 2 levels Pool of Human sera with chemical additives (preservatives)	Vials (liquid) Human serum with chemical additives (preservatives)
Format	Liquid	Liquid
Packaging	Kit composed of : Level 1: 2 x 1 ml vial (blue cap) Level 2: 2 x 1 ml vial (red cap)	Kit composed of : 4 x 1 ml vial

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

- CLSI - Evaluation of Precision Performance of Clinical Chemistry Devices - EP05-A2
- CLSI - Evaluation of the Linearity of Quantitative Analytical Methods - EP06-A
- CLSI - Method Comparison and Bias Estimation Using Patient Samples - EP09-A2
- CLSI - Protocols for Determination of Limits of Detection and Limits of Quantitation - EP17-A

L. Test Principle:

ABX Pentra CRP CP is a latex-enhanced immunoturbidimetric assay developed to measure CRP levels in serum and plasma samples for conventional CRP ranges.

When an antigen-antibody reaction occurs between CRP in a sample and anti-CRP antibody which has been sensitized to latex particles, agglutination results. This agglutination is detected as an absorbance change, with the magnitude of the change being proportional to the quantity of CRP in the sample. The actual concentration is then determined by interpolation from a calibration curve prepared from calibrators of known concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-run precision

5 specimens of very low, low, medium and high concentration and 3 controls were tested 20 times.

	Mean value mg/l	CV %
Control specimen 1	8.54	0.74
Control specimen 2	22.16	1.08
Control specimen 3	0.98	3.07
Specimen 1	0.86	4.15
Specimen 2	8.13	1.55
Specimen 3	18.66	0.92
Specimen 4	46.83	1.02
Specimen 5	126.11	2.25

Total precision

3 specimens of low, medium and high levels and 3 controls were tested in duplicate for 20 days (2 series per day)

	Mean value mg/l	CV %
Control specimen 1	8.46	4.31
Control specimen 2	21.88	2.17
Control specimen 3	1.23	5.57
Specimen 1	62.25	2.32
Specimen 2	124.14	2.92
Specimen 3	0.86	7.04

b. *Linearity/assay reportable range:*

The assay confirmed a measuring range from 1.0 mg/l to 160.0 mg/l, with an automatic post dilution up to 800 mg/l. These claims were established by the method comparison study described in section 2 below and confirmed by linearity and post dilution studies. The linearity data submitted is summarized below:

Linearity test	Dilution	Theoretical concentration	mean
Lower range	0.0625	0.64	0.37
	0.1250	1.29	0.93
	0.2500	2.57	2.33
	0.3750	3.86	3.68
	0.5000	5.15	5.14
	0.6250	6.43	6.42
	0.7500	7.72	7.81
	0.8750	9.01	9.04
	0.9350	9.63	9.62
	1.0000	10.30	10.30
Middle Range	0.10	5.12	5.14
	0.20	10.24	10.71
	0.30	15.35	15.83
	0.40	20.47	20.37
	0.50	25.59	25.67
	0.60	30.71	30.78
	0.70	35.82	35.68
	0.80	40.94	40.97
	0.90	46.06	46.06
	1.00	51.18	51.18
Upper Range	0.125	20.00	20.33
	0.250	40.00	39.3375
	0.375	60.00	59.1625
	0.500	80.00	82.7275
	0.625	100.00	104.3625
	0.750	120.00	124.7
	0.875	140.00	142.735
	0.938	150.00	152.875
	1.000	160.00	ND

Post-dilution Study

A post-dilution (factor = 1/5) will be initiated in cases of sample concentration above 160 mg/l. For the samples tested the relative bias was lower than +/- 10% over the range tested (160 – 726 mg/l).

Hook effect

No high dose hook effect was observed up to a concentration of 200 mg/l. A “Reaction Limit” alarm is calculated to flag samples which have an initial reaction speed higher than the highest calibrator point (160 mg/l). In these cases a post-dilution will be preformed.

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

ABX Pentra CRP Cal

Traceability - Determined using primary calibration with CRM n°470-CAP/IFCC, lot. 91/06-19. - The assigned values are indicated on each vial (5 levels with targeted values of 2.5, 10, 40, 80 and 160 mg/l)

Closed stability: 12 months at 2-10°C

Open stability: 3 months at 2-10°C

Based on real time stability studies

ABX Pentra Immuno I Control L/H

The assigned values specified are determined by calculating the mean value obtained from multiple determinations. The assigned values for both Low and High controls are lot-specific.

Closed stability: 24 months at 2-10°C

Open stability after reconstitution: 2 weeks at 2-10°C
3 months at -20°C

Based on real time stability studies

ABX Pentra Low CRP Control

The assigned values specified are determined by calculating the mean value obtained from multiple determinations. The assigned values for both Low and High controls are lot-specific.

Closed stability: 12 months at 2-10°C

Open stability: 4 weeks at 2-10°C

Based on real time stability studies

d. Detection limit:

The detection limit of this device (the lower range of measurement) was determined to be 1.0 mg/l.

e. Analytical specificity:

Hemoglobin up to 485 mg/dl, total bilirubin up to 16.9 mg/dl, direct bilirubin up to 18.8 mg/dl, and triglycerides (as Intralipid ®, representative of lipemia) up to 612.5 mg/dl do not interfere with CRP determination by this test.

Study method:

The above substances were added to the base serum at two different CRP concentration (approx 8.6 mg/l and 27.36 mg/L). The base serum with each substance was then serially diluted with the same base serum that was added saline instead of substance to adjust CRP concentration. The acceptance limit for non-interference was to be with-in 10% of the mean value of each level.

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

190 patient samples (serum) were tested with the device and a commercial reagent according to the recommendations found in the CLSI (NCCLS), EP9-A2 protocol.

Values ranged from 0.13 to 158.30 mg/l.

The equation for the regression line obtained was:
 $Y = 1.03x - 0.18$ with a correlation coefficient $r^2 = 0.997$.

b. Matrix comparison:

To demonstrate equivalence of CRP results in serum and Plasma Heparin-Lithium samples, comparison study was performed. Forty-nine (49) samples were evaluated on ABX Pentra 400 analyzer using ABX Pentra CRP CP reagent.

Serum versus Plasma equation for the regression line obtained was:
 $Y = 0.983x + 0.0194$ with a correlation coefficient $r^2 = 0.9992$

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:

Adults (20-60 years) < 5 mg/l determined by referenced literature

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.