

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

**A. 510(k) Number:**

k062180

**B. Purpose for Submission:**

New Device

**C. Measurand:**

$\alpha$  - Amylase

**D. Type of Test:**

Quantitative, enzymatic

**E. Applicant:**

Horiba ABX

**F. Proprietary and Established Names:**

Proprietary Name: ABX Pentra Amylase CP

Common Name:  $\alpha$  – Amylase

Proprietary Name: ABX Pentra N Control

Common Name: Quality Control

Proprietary Name: ABX Pentra P Control

Common Name: Quality Control

Proprietary Name: ABX Pentra MultiCal

Common Name: Calibrator

**G. Regulatory Information:**

1. Regulation section:

21 CFR § 862.1070 - Amylase test system  
21 CFR 862.1660 - Quality control material (assayed and unassayed)  
21 CFR 862.1150 - Calibrator

2. Classification:

Class II – reagent and calibrator  
Class I – controls

3. Product code:

JFJ – reagent  
JIX – calibrator  
JJY – controls

4. Panel:

Clinical Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

Refer to Indications for Use.

2. Indication(s) for use:

Amylase reagent, with associated calibrators and controls, are intended for use on ABX PENTRA 400 Clinical Chemistry Analyzer to measure amylase analyte.

ABX PENTRA Amylase CP reagent with associated calibrators and controls are for quantitative in vitro diagnostic determination of the activity of the enzyme amylase in human serum and plasma based on an enzymatic photometric assay.

Amylase measurements are used primarily for the diagnosis and treatment of pancreatitis (inflammation of the pancreas).

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

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

For use with the ABX PENTRA 400 analyzer only.

**I. Device Description:**

Reagent 1 consists of Good's buffer (0.1 mol/L), NaCl (62.5 mmol/L), MgCl<sub>2</sub> (12.5 mmol/L),  $\alpha$ -glucosidase ( $\geq 2.5$  kU/L), and sodium azide (< 1g/L).

Reagent 2 consists of Good's buffer (0.1 mol/L), 4,6-ethylidene-(G7)-p-nitrophenyl-(G1)- $\alpha$ -D-maltoheptaoside (8.5 mmol/L) and sodium azide (< 1g/L).

The ABX Pentra MultiCal is serum based and provided in lyophilized form. Users reconstitute the calibrator with 3 mL of deionized water. The MultiCal contains multiple analytes including amylase, which is obtained from porcine pancreas. The concentration or activities of the analytes are lot-specific.

The ABX Pentra N and P controls are serum based and provided in lyophilized form. Users reconstitute the controls with 5 mL of deionized water. The controls contain multiple analytes including amylase, which is obtained from porcine pancreas and human saliva. The concentration or activities of the analytes are lot-specific.

All human source materials were shown to be free from HBsAG and antibodies to HCV and HIV by FDA approved methods.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

COBAS Reagent for  $\alpha$ -Amylase  
ABX PENTRA N & P Control (amylase ranges added)  
ABX PENTRA N Multical (amylase ranges added)

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

k801295 (reagent)  
k052007 (calibrator and control)

3. Comparison with predicate:

Similarities - Reagent		
Item	Device	Predicate
Analyte	Alpha-amylase	Alpha-amylase
Method	Enzymatic photometric assay	Enzymatic photometric assay
Reagent components	Bi-reagent cassette, ready to use  REAGENT 1 : Good's buffer, NaCl, MgCl <sub>2</sub> , α-Glucosidase, Sodium azide  REAGENT 2 : Good's buffer, EPS-G7, Sodium azide	Single-reagent bottle, lyophilized  REAGENT : PNP7, Sodium chloride, Calcium chloride, α-Glucosidase (microbial), buffers, stabilizers, fillers and preservative
Format	Liquid	Liquid
Sample volume	4 µl/test	5 µl/test
Upper linearity limit	2000 U/l (6,000 U/L with automatic post-dilution)	2000 U/L (10,000 U/L with automatic post-dilution)
Closed reagent stability	24 months at 2-8°C	Until the expiration date when stored at 2-8°C
Open Reagent stability	on-board stability (refrigerated area): 42 days	after reconstitution: 30 days at 2-8C 4 days at 15-25°C

Differences - Reagent		
Item	Device	Predicate
Specimen	Serum, Plasma	Serum, Urine
Precision	CV Total < 2.74%	CV Total < 8.2%
Lower limit	4.5 U/l	15 U/l
Calibration stability	8 days	30 days

The controls and calibrators included in this submission are identical to the predicate devices.

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

Valtec guideline (Vassault *et al.*, Ann. Biol. Clin., 1986, (44), 686-745)

FDA Guidance Document: Guidance for Industry and FDA Staff : “Format for Traditional & Abbreviated 510(k)s” : August 12, 2005

FDA Guidance Document: In vitro diagnostics devices : Guidance for the preparation of 510(k) submissions Jan 1997

NCCLS (CLSI) EP-5A2: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline

NCCLS (CLSI) EP-6A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

NCCLS (CLSI) EP-9A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition

NCCLS (CLSI) EP-21A: Estimation of Total Analytical Error for Clinical Laboratory Methods; Approved Guideline

**L. Test Principle:**

The substrate 4,6-ethylidene-(G7)-p-nitrophenyl-(G1)- $\alpha$ -D-maltoheptaoside (EPS-G7) is cleaved by  $\alpha$ -amylases into various fragments. These are further hydrolyzed in a second step by  $\alpha$ -glucosidase producing glucose and p-nitrophenol. The increase in absorbance represents the total (pancreatic and salivary) amylase activity in the sample.

**M. Performance Characteristics:**1. Analytical performance:a. *Precision/Reproducibility:*

To evaluate within run precision, the sponsor selected two controls and three serum samples. Each sample was run 20 times in a single run with the following results:

	Control		Sample		
	Normal	Abnormal	Low	Medium	High
Mean (U/L)	74.6	180.6	50.0	89.2	258.4
SD	0.51	1.28	0.89	1.05	1.56
CV(%)	0.69	0.71	1.78	1.18	0.60

To evaluate between run and total precision, the sponsor followed CLSI EP-5A. Two controls and two serum samples were tested in duplicate for 20 days, with two replicates per day, for a total of four results per day and 80 results total for each sample. The following results were observed:

	Control		Sample	
	Normal	Abnormal	Low	High
Mean (U/L)	76.7	184.1	71.5	415.0
Within-Run SD	0.75	1.32	0.84	2.79
Within-Run CV	0.98	0.72	1.18	0.67
Total SD	2.07	3.21	1.96	7.19
Total CV	2.70	1.74	2.74	1.73
Between-Day SD	1.61	1.86	1.60	4.87
Between-Day CV	2.09	1.01	2.23	1.17
Between-Run SD	1.07	2.26	0.77	4.50
Between-Run CV	1.39	1.23	1.07	1.08

*b. Linearity/assay reportable range:*

To evaluate linearity and reportable range, the sponsor followed CLSI EP-6A. Two datasets were collected, one covering the lower range from approximately 7 – 150 U/L and another covering the upper range from approximately 100 – 2200 U/L. The CLSI guideline instructs users to examine whether a non-linear polynomial fits the data better than a linear one and then assess whether the difference between the two is less than the amount of allowable bias for the method. The sponsor did this, and determined that for both datasets the difference was less than their internal estimate of 8% allowable bias.

In addition, post dilution studies were performed to validate the automated dilution function and range.

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

Calibrator. The sponsor states that the Multical calibrator is traceable to the Institute for Reference Materials and Measurements (IRMM)/ International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference material 456 for amylase.

Real-time stability data has been provided at the recommended storage temperature for both open and closed vials. The acceptance criterion was recovery  $\pm$  5% of day 0 value.

Calibrator values are assigned by comparison to a master lot stored at -80° C. Deviations of up to 4% are allowed.

Controls. Real-time stability data has been provided at the recommended storage temperature for both open and closed vials. The acceptance criterion was recovery  $\pm 10\%$  of day 0 value.

Control values are assigned from the ABX PENTRA calibrator, reagents and analyzers. The target value is determined by the median of results from 150 measurements. Six analyzers are used over 5 days, with one calibration per day. 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  $\pm 3$  standard deviations.

d. *Detection limit:*

Method : In accordance with the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745)

Minimum Detection Limit (MDL) is calculated from 30 measurements of saline water (0.9 g/l)

Formula :  $MDL = \text{mean of measurements} + 4.65 \text{ SD}$  (mean of measurement = 0 when negative)

n	Values	n	Values
1	-1.1	16	-0.9
2	-0.8	17	-0.5
3	-0.3	18	-0.7
4	-2.8	19	-0.3
5	-0.9	20	-1.1
6	-1.6	21	0.4
7	-1.8	22	-2.1
8	-2	23	-2.6
9	-1.4	24	-1
10	-1	25	-1.2
11	-1.2	26	-1.3
12	-1.4	27	-0.7
13	-0.2	28	-1.6
14	-0.7	29	-4
15	-3.5	30	-1.6

Mean	<b>-1.33</b>
SD	<b>0.95</b>

Minimum Detection Limit =	Mean + 4,65 SD :
	<b>4 UI</b>

From the MDL value, the test range low assigned for this method and in the test instruction was calculated to be 4 U/L.

*e. Analytical specificity:*

Hemoglobin up to 278  $\mu\text{mol/l}$  (479 mg/dl), total bilirubin up to 450  $\mu\text{mol/l}$  (29 mg/dl), direct bilirubin up to 474  $\mu\text{mol/l}$  (27.7 mg/dl) and triglycerides (as Intralipid ®, representative of lipemia) up to 7 mmol/l (612.5 mg/dl) were tested by the sponsor and found not to interfere with Amylase determination by this method. Potential interferents were tested at two amylase concentrations. The sponsor defined non-interference as the following: within  $\pm 20$  U/L for the low concentration (approximately 136 U/L) and within  $\pm 50$  U/L for the high concentration test sample (approximately 287 U/L).

*f. Assay cut-off:*

Not Applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

Due to the difficulty of obtaining native samples covering the reportable range of the assay, the sponsor supplemented the native samples with both diluted and spiked samples, for a total of 131 samples. Each sample was analyzed in duplicate and the samples ranged in concentration from 4 to 1659 U/L by the predicate method. Linear regression was performed comparing the mean of predicate vs the mean of the new device, and the following line equation was calculated:

$$\text{Horiba ABX} = (*1.231 \text{ X predicate method}) - 26 \text{ U/L}$$

$$r = 0.9985$$

\*From the data provided, it appears that the positive bias increases as amylase values increase. However, this bias was judged to be clinically insignificant.

*b. Matrix comparison:*

To demonstrate comparable performance between serum and lithium-heparin plasma, the sponsor compared 70 paired serum and plasma samples on the Pentra 400 analyzer using the ABX Pentra Amylase CP reagent. The samples ranged in concentration from a low of 24 to a high of 255 U/L. Linear regression produced a slope of 1.00 with a y-intercept of -2.6 U/L. The correlation coefficient (r) was 0.998.

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:

Not Applicable

5. Expected values/Reference range:

< 100 U/L (both women and men)

Reference:

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, 4<sup>th</sup> ed.

**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.