

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

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

k060325

**B. Purpose for Submission:**

Notification of intent to manufacture and market the devices: a group of reagents and their associated controls and calibrators for use on the ABX PENTRA 400 - ABX PENTRA Bilirubin, Direct CP, ABX PENTRA Bilirubin, Total CP, ABX PENTRA N Control, ABX PENTRA P Control, and ABX PENTRA Multical.

**C. Measurand:**

Direct and Total Bilirubin

**D. Type of Test:**

Quantitative, colorimetric

**E. Applicant:**

Horiba ABX

**F. Proprietary and Established Names:**

Trade/Proprietary Name: ABX PENTRA Bilirubin Direct CP  
Common or Usual Name: Bilirubin, Direct

Trade/Proprietary Name: ABX PENTRA Bilirubin Total CP  
Common or Usual Name: Bilirubin, Total

Trade/Proprietary Name: ABX PENTRA N Control  
Common or Usual Name: Quality Control

Trade/Proprietary Name: ABX PENTRA P Control  
Common or Usual Name: Quality Control

Trade/Proprietary Name: ABX PENTRA N Multical  
Common or Usual Name: Calibrator

**G. Regulatory Information:**

1. Regulation section:

21 CFR 862.1110: Bilirubin (Total or Direct) test system

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

21 CFR 862.1150: Calibrator

2. Classification:

Class II - ABX PENTRA Bilirubin Direct CP, ABX PENTRA Bilirubin Total CP, ABX PENTRA N Multical

Class I - **ABX PENTRA N Control, ABX PENTRA P Control**

3. Product code:

ABX PENTRA Bilirubin Direct CP - CIG

ABX PENTRA Bilirubin Total CP- CIG

ABX PENTRA N Control - JJY

ABX PENTRA P Control - JJY

ABX PENTRA N Multical - JIX

4. Panel:

Chemistry

**H. Intended Use:**

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

ABX PENTRA Bilirubin, Direct CP reagent with associated calibrators and controls are for quantitative in vitro diagnostic determination of Direct Bilirubin in human serum and plasma based on a photometric test using 2,4-dichloroaniline (DCA) for use on ABX PENTRA 400 Clinical Chemistry Analyzer.

ABX PENTRA Bilirubin, Total CP reagent with associated calibrators and controls are for quantitative in vitro diagnostic determination of Total Bilirubin in human serum and plasma based on a photometric test using 2,4-dichloroaniline (DCA) and detergents for use on ABX PENTRA 400 Clinical Chemistry Analyzer.

Measurements of the levels of Bilirubin (Direct or Total), an organic compound formed during the normal and abnormal destruction of red blood cells, are used in the diagnosis and treatment of liver, hemolytic hematological, and metabolic disorders, including hepatitis and gall bladder block.

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.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

For use on the Horiba ABX PENTRA 400

## I. Device Description:

The **ABX PENTRA Bilirubin Direct CP** consists of a cassette containing two liquid reagents (1 – 24ml & 2 – 7ml). The **ABX PENTRA Bilirubin Total CP** consists of a cassette containing two liquid reagents (1 – 44ml & 2 – 14ml)

The **ABX PENTRA N Multical** is a 3 level serum based calibrator for use in the calibration of quantitative Horiba ABX PENTRA Bilirubin Total and Direct CP methods on Horiba ABX clinical chemistry analyzers as specified on the vials.

The **ABX PENTRA N & P Controls** are serum based liquids for use in quality control by monitoring accuracy and precision for the quantitative ABX PENTRA Bilirubin Total and Direct CP methods as specified in the enclosed package insert.

The **ABX PENTRA N Multical** and **ABX PENTRA N & P Controls** are prepared from a human blood-based matrix.

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):

Roche Reagent for Direct Bilirubin, Roche Reagent for Total Bilirubin  
ABX PENTRA N & P Control (Total and Direct Bilirubin ranges added)  
ABX PENTRA N Multical (Total and Direct Bilirubin ranges added)

### 2. Predicate 510(k) number(s): k910593, k910591

k910593 – Direct Bilirubin  
k910591 – Total Bilirubin  
k052007 ABX PENTRA Control and Calibrator

### 3. Comparison with predicate:

|                | Predicate device<br>(k910593): | Device : Direct<br>Bilirubin      |
|----------------|--------------------------------|-----------------------------------|
| Device<br>Name | Direct Bilirubin               | ABX PENTRA<br>Bilirubin Direct CP |
| Instrument     | COBAS Mira                     | HORIBA ABX                        |
| Analytes       | Direct Bilirubin               | Direct Bilirubin                  |

|                    | <b>Predicate device<br/>(k910593):</b>                                      | <b>Device : Direct<br/>Bilirubin</b>                      |
|--------------------|---|---|
| <b>Method</b>      | Photometric using diazotized sulfanilic acid                                | Photometric using 2,4-dichloroaniline                     |
| <b>Specimen</b>    | Serum   | Serum, Plasma   |
| <b>Format</b>      | Liquid  | Liquid  |
| <b>Packaging</b>   | Single reagent bottles  | Bi-reagent cassette                                       |
| <b>Controls</b>    | Commercially available  | Recommended ABX PENTRA N and P controls                   |
| <b>Calibrators</b> | Factor method: uses the factor generated during Total Bilirubin calibration | Uses recommended calibration material ABX PENTRA Multical |

|                        | <b>Predicate device<br/>(k910591):</b>  | <b>Device : Total<br/>Bilirubin</b>  |
|------------------------|---|--|
| <b>Device Name</b>     | <b>Total Bilirubin</b>  | <b>ABX PENTRA Bilirubin, Total CP</b>  |
| <b>Manufactured by</b> | Roche, USA  | HORIBA ABX, France   |
| <b>Instrument</b>      | COBAS MIRA chemistry system   | ABX PENTRA 400   |
| <b>Analytes</b>        | Total bilirubin   | Total bilirubin  |
| <b>Method :</b>        | Photometric test using diazotized sulfanilic acid, and dimethylsulfoxide (DMSO) and ethylene glycol as solvents | Photometric test using 2,4-dichloroaniline (DCA), and a specific mixture of detergents |
| <b>Specimen :</b>      | Serum   | Serum<br>Plasma  |
| <b>Format</b>          | Liquid  | Liquid   |
| <b>Packaging</b>       | Single-reagent bottles  | Bi-reagent cassette  |
| <b>Calibrators</b>     | Commercially available calibration material (not included)  | Recommended calibration material (not included): ABX Pentra Multical                   |

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

The following standards & FDA guidance documents have been used to support this submission

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

“In vitro diagnostic devices : Guidance for the preparation of 510(k) submissions Jan 1997”

“Guidance for Industry and FDA Staff Bundling Multiple Devices or Multiple Indications in a Single Submission, November 2003”

CLSI (NCCLS) :

i) EP5-A2 – Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition

ii) EP6-A - Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline

iii) EP9-A2 – Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline -Second Edition

iv) EP21-A - Estimation of Total Analytical Error for Clinical Laboratory Methods; Approved Guideline

#### **L. Test Principle:**

Di-azoamine Dye, Colorimetric assay, the presence of bilirubin (total or direct) in plasma or serum combined with 2, 4-dichloroaniline (DCA) results in the formation of a Diazoamine dye which is proportional to bilirubin concentration.

#### **M. Performance Characteristics (if/when applicable):**

##### **1. Analytical performance:**

##### ***a. Precision/Reproducibility:***

##### **ABX PENTRA Bilirubin Direct CP**

##### **Within Run Precision:**

**Method:** Based upon the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986,

(44), 686-745); 2 controls (as above) and 3 specimens of low, medium and high concentrations were tested 20 times in a single run for each sample. (note: Human High Sample was done with dilution)

| Material     | Mean (mg/dL) | SD (mg/dL) | CV%  |
|--------------|--------------|------------|------|
| Control N    | 0.90         | 0.01       | 0.67 |
| Control P    | 1.85         | 0.01       | 0.44 |
| Human Low    | 0.23         | 0.01       | 3.23 |
| Human Medium | 1.52         | 0.01       | 0.59 |
| Human High   | 7.88         | 0.21       | 2.69 |

#### Between run and Total Precision

Method: Based upon CLSI/NCCLS EP-5A, two specimens of low & high levels and 2 controls were tested in duplicate for 20 days, two series per day. (n=80)

| Material  | Mean (mg/dL) | SD (mg/dL) | CV%  |
|-----------|--------------|------------|------|
| N Control | 0.94         | 0.04       | 4.26 |
| P Control | 2.02         | 0.09       | 4.22 |
| Sample 1  | 0.69         | 0.02       | 3.27 |
| Sample 2  | 3.83         | 0.11       | 2.98 |

#### **ABX Pentra Bilirubin, Total CP**

##### Within Run Precision

Based upon the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745); 2 controls (as above) and 3 specimens of low, medium and high concentrations were tested 20 times in a single run for each sample.

| Material     | Mean (mg/dL) | SD (mg/dL) | CV%  |
|--------------|--------------|------------|------|
| Control N    | 0.97         | 0.02       | 1.77 |
| Control P    | 5.35         | 0.04       | 0.66 |
| Human Low    | 0.91         | 0.02       | 2.51 |
| Human Medium | 3.25         | 0.03       | 0.90 |
| Human High   | 8.73         | 0.05       | 0.60 |

### Between run and Total Precision

Based upon NCCLS (CLSI) EP-5A, two specimens of low & high levels and 2 controls were tested in duplicate for 20 days, two series per day. N=80

| Material   | Mean (mg/dL) | SD (mg/dL) | CV%  |
|------------|--------------|------------|------|
| Control N  | 1.04         | 0.03       | 3.35 |
| Control P  | 4.30         | 0.09       | 1.98 |
| Human Low  | 3.03         | 0.06       | 1.88 |
| Human High | 8.51         | 0.13       | 1.55 |

#### *b. Linearity/assay reportable range:*

##### **ABX PENTRA Bilirubin Direct CP**

Linearity studies across the measuring range were performed via protocols based upon CLSI EP6-A. The studies demonstrated linearity of the assays and the linear statistics listed below. In addition, post dilution studies were performed to validate the automated dilution function and range.

##### **ABX PENTRA Bilirubin Direct CP**

The measuring range of the assay is 0.69 to 6.79 mg/dl. Post dilution up to 33.0 mg/dL.

Linear regression statistics:  $y = 0.9279x + 1.8604$   $r^2 = 0.9976$

##### **ABX Pentra Bilirubin, Total CP**

The measuring range of the assay is 0.20 to 26.30 mg/dl. Post dilution up to 181.5 mg/dL.

Linear regression statistics:  $y = 0.9037x + 0.9705$   $r^2 = 0.9988$

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

##### **Sample stability**

The sponsor states the following related to sample stability:

Exposure to sunlight may result in a decrease in total bilirubin by up to 30% after 1 hour.

At normal room temperature and protected from light exposure stable for 3 days.

Reference:

Thomas L. Clinical Laboratory Diagnostics. 1<sup>st</sup> ed. Frankfurt: TH-Books Verlagsgesellschaft; 1998. p. 192-202.

### **ABX PENTRA Bilirubin Direct CP**

*Reagent Shelf-life:* Real time stability of the reagent stored at 2-8°C has been evaluated on 3 different lots. Results support a real time stability of 18 months.

*Reagent Stability on board:* Reagent stability on-board has been evaluated testing accuracy and linearity periodically. The results support reagent stability on-board (refrigerated) after opening of 25 days.

### **ABX PENTRA Bilirubin, Total CP**

*Reagent Shelf-life:* Real time stability of the reagent stored at 2-8°C has been evaluated on 3 different lots. Results support a real time stability of 18 months.

*Reagent Stability on board:* Reagent stability on-board has been evaluated testing accuracy and linearity periodically. The results support reagent stability on-board (refrigerated) after opening of 25 days.

### **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/parameter. 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).

### **ABX Pentra Multical traceability**

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/parameter.

### **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:*

**ABX PENTRA Bilirubin Direct CP**

Minimum Detection Limit (MDL) was calculated from 30 measurements of saline water (0.9 g/l) using the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745). The claimed MDL value is 0.69 mg/dl.

**ABX Pentra Bilirubin, Total CP**

Minimum Detection Limit (MDL) was calculated from 30 measurements of saline water (0.9 g/l) using the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745). The claimed MDL value is 0.20 mg/dl.

*e. Analytical specificity:*

**ABX PENTRA Bilirubin Direct CP**

Study materials: Hemoglobin and triglycerides (as Intralipid ®, representative of lipemia) were added to pooled Human serum at two different direct bilirubin concentrations (normal and high). The base serum with each substance was then serially diluted with unspiked base serum to adjust direct bilirubin concentration.

Method: Based upon the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745); specimens of low, medium and high concentrations were tested 20 times in a single run for each sample.

Due to hemoglobin interference, hemolyzed samples should not be used.

**ABX Pentra Bilirubin, Total CP**

Study materials: Hemoglobin up to 220 µmol/L (380 mg/dL) and triglycerides (as Intralipid ®, representative of lipemia) up to 7 mmol/L (612.5 mg/dL) were added to pooled Human serum at two different direct bilirubin concentrations (normal and high). The base serum with each substance was then serially diluted with unspiked base serum to adjust direct bilirubin concentration

Method: Method: Based upon the Valtec guideline (Vassault et al., Ann. Biol. Clin., 1986, (44), 686-745); specimens of low, medium and high concentrations were tested 20 times in a single run for each sample.

Hemoglobin up to 220 µmol/L (380 mg/dL) and triglycerides (as Intralipid ®, representative of lipemia) up to 7 mmol/L (612.5 mg/dL) do not interfere with total bilirubin determination by this test.

*f. Assay cut-off:*

Not applicable

## 2. Comparison studies:

### a. *Method comparison with predicate device:*

#### **ABX PENTRA Bilirubin Direct CP**

A total of 110 samples were compared with the Roche Direct Bilirubin reagent (predicate) on the Roche MIRA Plus.

$$Y = 1.0571x - 1.0551, r^2 = 0.9974$$

#### **ABX Pentra Bilirubin, Total CP**

A total of 106 samples were compared with the Roche Total Bilirubin reagent (predicate) on the Roche MIRA Plus.

$$Y = 1.0303x - 2.7861, r^2 = 0.9961$$

### b. *Matrix comparison:*

#### **ABX PENTRA Bilirubin Direct CP**

To demonstrate equivalence of direct bilirubin results in serum and Plasma Heparin-Lithium samples, comparison study was performed. 39 matched samples were evaluated on ABX Pentra 400 analyzer using ABX Pentra Bilirubin, Direct CP reagent.  $Y = 0.9981x + 0.0837, r^2 = 0.9693$ . The results show that there is no significant difference between serum specimens and Heparin-Lithium Plasma.

#### **ABX Pentra Bilirubin, Total CP**

To demonstrate equivalence of total bilirubin results in serum and Plasma Heparin-Lithium samples, comparison study was performed. 39 samples were evaluated on Pentra 400 analyzer using ABX Pentra Bilirubin, Total CP reagent.  $Y = 0.9917x + 0.0577, r^2 = 0.9779$ . The results show that there is no significant difference between serum specimens and Heparin-Lithium Plasma.

## 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:

**ABX PENTRA Bilirubin Direct CP**

Adults and children: 0 - 0.2 mg/dL (0 - 3.4  $\mu$ mol/L).

Reference:

Thomas L. ed. Clinical Laboratory Diagnostics. 1<sup>st</sup> ed. Frankfurt: TH-Books Verlagsgesellschaft, 1998. p 192-202.

**ABX Pentra Bilirubin, Total CP**

**Adults: 0.1 – 1.2 mg/dL (1.7 – 21  $\mu$ mol/L**

Reference:

Thomas L. ed. Clinical Laboratory Diagnostics. 1<sup>st</sup> ed. Frankfurt: TH-Books Verlagsgesellschaft, 1998. p 192-202.

**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.