

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

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

K040391

**B. Purpose for Submission:**

Clearance of two sets of secondary reagents

**C. Analyte:**

Total and Direct Bilirubin

**D. Type of Test:**

Quantitative Colorimetric Assay

**E. Applicant:**

Pointe Scientific, Inc.

**F. Proprietary and Established Names:**

Hitachi Direct Bilirubin Reagent

Hitachi Total Bilirubin Reagent

**G. Regulatory Information:**

1. Regulation section:  
21 CFR § 862.1110, Bilirubin (total or direct) test system
2. Classification:  
Class II
3. Product Code:  
CIG, Diazo Colorimetry, Bilirubin
4. Panel:  
Clinical Chemistry (75)

**H. Intended Use:**

1. Intended use(s):

The Pointe Scientific Direct and Total Bilirubin assays are to be used in a diagnostic laboratory setting, by qualified laboratory technologists, for the quantitative determination of Direct or Total Bilirubin in human serum. They are intended for in vitro diagnostic use only.

Direct and Total bilirubin measurements provide information to assist in assessment of liver function and conditions such as hemolytic and obstructive jaundice.

2. Indication(s) for use:  
See intended use
3. Special condition for use statement(s):  
For professional prescription use only
4. Special instrument Requirements:  
Hitachi clinical chemistry analyzers (validated on Hitachi 704, 717, 747, 911, 912 analyzers)

### I. Device Description:

Both the Total and Direct bilirubin reagents consist of two ready-to-use liquid reagents (see device comparison below for information on their make-up).

### J. Substantial Equivalence Information:

1. Predicate device name(s):  
Roche Total Bilirubin Reagent and Roche Direct Bilirubin Reagent
2. Predicate K number(s):  
K910591 and K910593, respectively
3. Comparison with predicate:

The devices share the same intended use with their predicates.

#### Total Bilirubin:

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Assay Range	0 – 30 mg/dL	0 – 20 mg/dL
Reagents	Reagent 1: Acid buffer 50 mmol/L Reagent 2: Acid Buffer >30 mmol/L, >2.0 mmol/L DPD Stabilizers	Reagent 1: Sulfanilic Acid 32.2 mmol/L, DMSO, Ethylene glycol, buffers, stabilizers Reagent 2: Sodium Nitrite 109 mmol/L, buffers, fillers, stabilizers

#### Direct Bilirubin:

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Assay range	0 – 10 mg/dL	0 – 20 mg/dL
Reagents	Reagent 1: Acid buffer 50 mmol/L Reagent 2: Acid Buffer >30 mmol/L, >2.0 mmol/L DPD Stabilizers	Reagent 1: Hydrochloric acid 0.05 mol/L Reagent 2: Sulfanilic acid 25.7 mmol/L, Hydrochloric acid 0.7 mol/L, Sodium Nitrite 2.7 mmol/L, Sodium Bicarbonate 13.9 mmol/L

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

NCCLS Guideline EP5-A - Evaluation of Precision Performance of Clinical Chemistry Devices

**L. Test Principle:**

Azobilirubin is produced when bilirubin in the sample is coupled with a diazonium salt (DPD) in a strongly acidic medium. The amount of azobilirubin produced can be measured spectrophotometrically and is proportional to the bilirubin concentration in the sample.

**M. Performance Characteristics (if/when applicable):**1. Analytical performance:*a. Precision/Reproducibility:*

Assay imprecision was tested according to NCCLS Guideline EP5-A. Samples were assayed in duplicate twice per day for 20 days. Results are summarized below (units = mg/dL):

Total Bilirubin:

	Within Day			Total		
	Mean	SD	% CV	Mean	SD	% CV
<b>Sample 1</b>	1.0	0.037	3.61	1.0	0.043	4.24
<b>Sample 2</b>	5.8	0.060	1.04	5.8	0.085	1.46

Direct Bilirubin:

	Within Day			Total		
	Mean	SD	% CV	Mean	SD	% CV
<b>Sample 1</b>	1.0	0.0042	2.01	1.9	0.088	4.57
<b>Sample 2</b>	5.5	0.074	1.35	5.8	0.082	1.51

*b. Linearity/assay reportable range:*

To evaluate assay linearity, samples from a commercially available linearity set were assayed in duplicate and the mean recovered value was plotted against the expected value. Results are summarized as follows:

Total Bilirubin: Observed = (0.99703)Expected + 0.23428  
Range Tested = 0.5 to 20.5 mg/dL

Direct Bilirubin: Observed = (1.0241)Expected – 0.38489  
Range Tested = 0.5 to 20.5 mg/dL

The reportable range of the Total Bilirubin assay is 0.1 to 30 mg/dL. The reportable range of the Direct Bilirubin assay is 0.1 to 10 mg/dL. Assay results for both assays that are below 0.1 should be reported as <0.1 mg/dL.

*c. Traceability (controls, calibrators, or method):*

The package insert recommends that quality control be performed using control sera with known bilirubin values.

*d. Detection limit:*

The sensitivity of the assay is defined as the  $\Delta A/\text{mg/dL}$  and is 0.086/mg/dL for the Total Bilirubin assay and 0.016/mg/dL for the Direct Bilirubin assay.

*e. Analytical specificity:*

Non-interference is defined as recovery within +/- 10%:

Triglycerides up to 1000 mg/dL and Hemoglobin up to 500 mg/dL do not significantly interfere with the Total Bilirubin assay.

Triglycerides up to 500 mg/dL and Hemoglobin up to 100 mg/dL do not significantly interfere with the Direct Bilirubin assay.

*f. Assay cut-off:*  
Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

**Total Bilirubin:**

Seventy-six (76) serum samples (2 controls, 5 linearity standards, 11 spiked serum samples, 48 normal samples, and 10 elevated samples) were evaluated on the device and the predicate. Samples with concentrations above the useable range of the predicate device were diluted 1:1 with saline for measurement on the predicate assay. The resulting regression statistics were Device = 1.01(Predicate) + 0.09,  $r = 0.999$ .

**Direct Bilirubin:**

Sixty-two (62) serum samples (2 controls, 3 linearity standards, 5 spiked serum samples, 48 normal samples, and 4 elevated samples) were evaluated on the device and the predicate. The resulting regression statistics were Device = 1.02(Predicate) - 0.07,  $r = 0.996$ .

*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:

Total Bilirubin:

Adults and Infants older than 1 month: 0.2 – 1.0 mg/dL

Infants: Full Term Newborn

Up to 24hrs: 2.0 to 6.0 mg/dL

Up to 48 hrs: 6.0 to 10.0 mg/dL

Days 3-5: 4.8 to 8.0 mg/dL

Direct Bilirubin:

Adults and Infants older than 1 month: 0 – 0.5 mg/dL

The sponsor recommends that laboratories establish their own normal reference ranges for their demographics.

**N. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.