

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

A. 510(k) Number:

k050266

B. Purpose for Submission:

Notification of intent to introduce into interstate commerce, for commercial distribution, an in vitro diagnostic test for professional use.

C. Measurand:

Bilirubin, Total and Direct

D. Type of Test:

Enzymatic colorimetric

E. Applicant:

Stanbio Laboratory.

F. Proprietary and Established Names:

Classification name – Direct Bilirubin Test, Total Bilirubin Test

Proprietary name – Direct Bilirubin LiquiColor®, Total Bilirubin LiquiColor®

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1110 (Bilirubin total or direct) test system

2. Classification:

Class II

3. Product code:

JFM

4. Panel:

75, Chemistry

H. Intended Use:

1. Intended use(s):

See indication for use below.

2. Indication(s) for use:

The Stanbio Direct Bilirubin LiquiColor® and Total Bilirubin LiquiColor® test systems are devices intended for to measure levels of bilirubin (direct and total) in serum and plasma. Measurements of levels of bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, if used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and gall bladder block.

3. Special conditions for use statement(s):

This is an in vitro diagnostic test for professional use only.

4. Special instrument requirements:

A minimum of a spectrophotometer capable of absorbance readings at 540nm is required.

I. Device Description:

The Stanbio Direct Bilirubin LiquiColor® test kit is comprised of two reagents, Reagent 1 (R1) and Reagent 2. Each reagent also contains stabilizers and/or buffers. To calibrate the test kit, a calibrator is used that has values determined by a similar method.

The Stanbio Total Bilirubin LiquiColor® test kit is comprised of two reagents, Reagent 1 (R1) and Reagent 2. Each reagent also contains stabilizers and/or buffers. To calibrate the test kit, a calibrator is used that has values determined by a similar method.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Direct Bilirubin - Roche Diagnostics
Total Bilirubin - Roche Diagnostics

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

Direct Bilirubin – k910593
Total Bilirubin – k910591

3. Comparison with predicate:

| | Stanbio Direct Bilirubin LiquiColor | Roche Direct Bilirubin |
|--|--|--|
| Test Methodology | 2,4-Dichloroaniline | Diazotized sulfanilic acid |
| Intended Use | For the quantitative determination of Direct Bilirubin in serum and plasma. | For the quantitative determination of Direct Bilirubin in serum. |
| Linearity | 0.1 to 10 mg/dL | 0.05 to 20 mg/dL |
| Wavelength | 540 nm | 550 nm |
| Interferences | Ascorbic Acid – up to 30 mg/dL Hemoglobin – up to 10 mg/dL Lipemia – up to 2000 mg/dL Triglycerides | Hemoglobin – dependent upon the concentration of bilirubin in sample Lipemia – an increase of 0.4 mg/dL was found in serum with 0.1 mg/dL Direct Bilirubin when 533 mg/dL added of Intralipid |
| Accuracy/Correlation (Serum) | $y = 0.9393x - 0.06; r = 0.995$ | $y = 0.887x + 0.14; r = 0.995$ |
| Accuracy/Correlation (Plasma vs. Serum) | $y = 1.0118x - 0.0078; r = 0.9999$ | Not applicable |
| Storage | 2 – 8 °C | 2 – 8 °C |

| | Stanbio Total Bilirubin LiquiColor | Roche Total Bilirubin |
|--|---|--|
| Test Methodology | 2,4-Dichloroaniline | Diazotized sulfanilic acid |
| Intended Use | For the quantitative determination of Total Bilirubin in serum and plasma. | For the quantitative determination of Total Bilirubin in serum. |
| Linearity | 0.07 to 30 mg/dL | 0.1 to 22 mg/dL |
| Wavelength | 540 nm | 550 nm |
| Interferences | Ascorbic Acid – up to 30 mg/dL Hemoglobin – up to 500 mg/dL Lipemia – up to 2000 mg/dL Triglycerides | Hemoglobin – dependent upon the concentration of bilirubin in sample Lipemia – an increase of 0.4 mg/dL was found in serum with 0.2 mg/dL Direct Bilirubin when 333 mg/dL added of Intralipid |
| Performance Characteristics | | |
| Accuracy/Correlation (Serum) | $y = 1.0108x - 0.0145;$ $r = 0.995$ | $y = 1.082x + 0.024;$ $r = 0.998$ |
| Accuracy/Correlation (Plasma vs. Serum) | $y = 1.02x - 0.006; r = 0.9995$ | Not applicable |
| Storage | 2 – 8 °C | 2 – 8 °C |

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

Linearity was performed based upon the NCCLS guideline EP6-P2: *Evaluation of the Linearity of Quantitative Analytical Methods*. Precision was performed based on NCCLS EP5-A2: *Evaluation of Precision Performance of Clinical Chemistry Devices*.

L. Test Principle:

The Stanbio method for Direct Bilirubin LiquiColor® and Total Bilirubin LiquiColor® employs an enzymatic method.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Intra-assay precision for Direct and Total Bilirubin were performed with 20 replicates in a single run on an EPOS 5060 analyzer.

Direct Bilirubin

| Sample Number | Mean mg/dL | SD mg/dL | CV % |
|---------------|------------|----------|------|
| 1 | 0.36 | 0.01 | 3.12 |
| 2 | 0.76 | 0,01 | 1.46 |
| 3 | 2.07 | 0.03 | 1.30 |

Total Bilirubin

| Sample Number | Mean mg/dL | SD mg/dL | CV % |
|---------------|------------|----------|------|
| 1 | 0.89 | 0.03 | 3.05 |
| 2 | 1.02 | 0.02 | 2.32 |
| 3 | 4.83 | 0.05 | 0.95 |

Inter-assay precision for Direct and Total bilirubin were performed with duplicate samples in two runs per day for five days on an EPOS 5060 analyzer.

Direct Bilirubin

| Sample Number | Mean mg/dL | SD mg/dL | CV % |
|---------------|------------|----------|------|
| 1 | 0.35 | 0.01 | 3.34 |
| 2 | 0.75 | 0.01 | 1.00 |
| 3 | 2.13 | 0.02 | 0.71 |

Total Bilirubin

| Sample Number | Mean | SD | CV |
|---------------|-------|-------|------|
| | Mg/dL | Mg/dL | % |
| 1 | 0.87 | 0.02 | 2.74 |
| 2 | 1.15 | 0.04 | 3.49 |
| 3 | 4.65 | 0.13 | 2.86 |

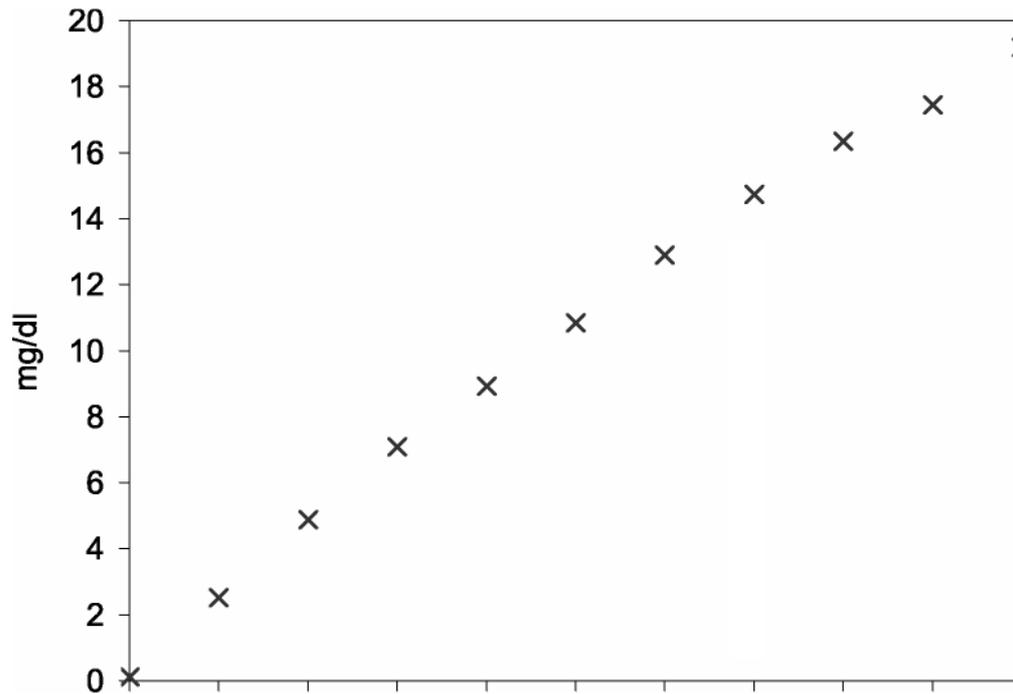
b. Linearity/assay reportable range:

Linearity studies were performed based upon the guidelines set forth in NCCLS EP6-P2: *Evaluation of the Linearity of Quantitative Analytical Methods*.

Direct Bilirubin

| | | |
|-----------------------|-------------------------------|----------------|
| Stanbio Laboratory | Direct Bilirubin Linearity | EPOS 5060 37°C |
|-----------------------|-------------------------------|----------------|

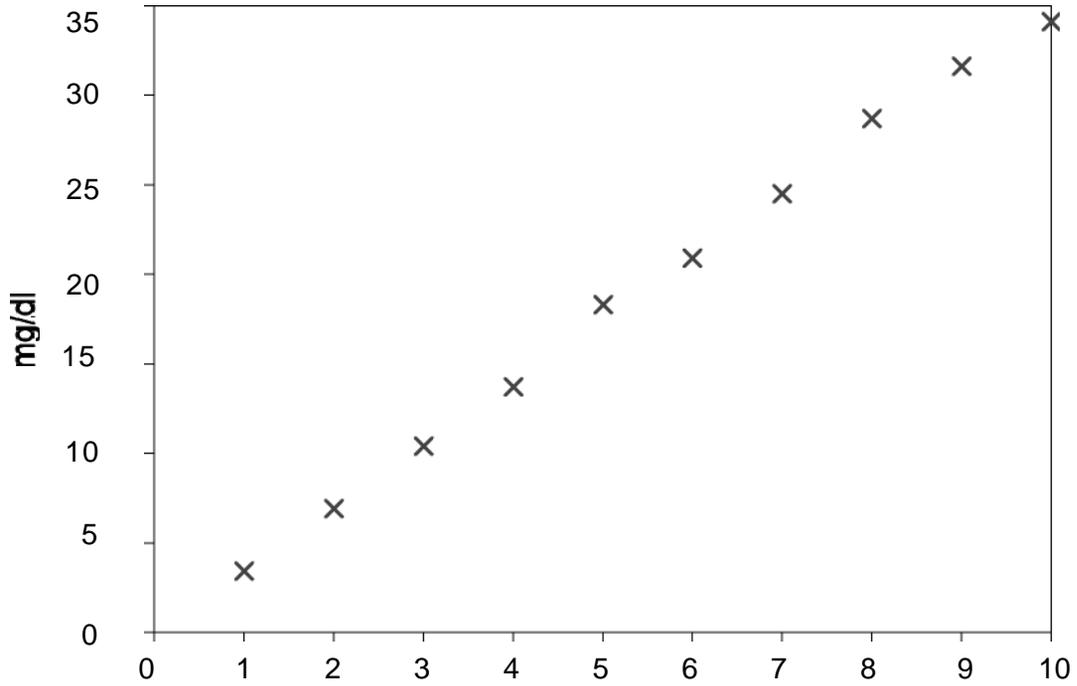
Linearity



| Dilution steps | Measured value in mg/dl |
|----------------|-------------------------|
| 0 | 0.11 |
| 1 | 2.51 |
| 2 | 4.88 |
| 3 | 7.08 |
| 4 | 8.92 |
| 5 | 10.85 |
| 6 | 12.89 |
| 7 | 14.74 |
| 8 | 16.34 |
| 9 | 17.44 |
| 10 | 19.19 |

Total Bilirubin

| | | |
|-----------------------|---------------------------|-----------------|
| Stanbio Laboratory | Total Bilirubin Linearity | EPOS 5060 37° C |
|-----------------------|---------------------------|-----------------|



| dilution steps | measured values in mg/dl |
|----------------|--------------------------|
| 0 | 0.05 |
| 1 | 3.41 |
| 2 | 6.92 |
| 3 | 10.4 |
| 4 | 13.7 |
| 5 | 18.3 |
| 6 | 20.9 |
| 7 | 24.50 |
| 8 | 28.7 |
| 9 | 31.6 |
| 10 | 34.1 |

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

The stability performance was determined by performing analysis on controls (normal and abnormal levels) over real time for 20 months. (Assigned expiration date of 20 months.)

The control recovery shall be within +/- 10% of the established mean value.

Open vial stability was established on board the analyzer to support a 30 day claim.

d. *Detection limit:*

The lower limit of detection was determined by injecting deionized water 10 times. A mean was determined and the standard deviation (SD) was calculated. From this determination, a 3 SD was calculated and then this value was added to the mean value. The final calculated value was defined as the lower limit of detection as performed above and the lower concentration measured multiple times in the linearity study.

The upper range of the assays was determined by looking at the graphical representation of the analyte concentration versus its dilution level. Looking at the graph and observing where the "line" breaks (is non-linear) is the point at which the cut-off is determined.

e. *Analytical specificity:*

No interference was observed by ascorbic acid up to 30 mg/dL, hemoglobin up to 500 mg/dL, and lipemia up to 2000 mg/dL triglycerides when measured using a triglyceride concentrate and up to 1000 mg/dL when measured using Intralipid. An extensive list of drugs or other agents interfering with bilirubin methodologies has been reported by Young et al.

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Direct bilirubin

Determination of bilirubin by the Stanbio Inc Direct Bilirubin (y) and by the predicate device (x) by using a combination of 75 true and 10 spiked human serum samples (n=85). The comparison was performed

on the EPOS 5060 and gave the following results $y=0.94x-0.06$ mg/dL, $r=0.995$.

Total Bilirubin

Determination of bilirubin by the Stanbio Inc Total Bilirubin assay Direct Bilirubin (y) and by the predicate device (x) by using a combination of 227 true and 20 spiked serum samples (n=247). The comparison was performed on the EPOS 5060 and gave the following results $y=1.01x-0.014$ mg/dL, $r=0.999$.

b. *Matrix comparison:*

Direct Bilirubin

Comparison of serum vs. plasma was carried out with 16 true and 6 spiked human samples (n=22) spanning the range of 0.1 to 11 mg/dL. The comparison was performed on the EPOS 5060 analyzer and gave the following results $y=1.01x-0.01$ mg/dL, $r=0.999$.

Total Bilirubin

Comparison of serum vs. plasma was carried out with 11 true and 8 spiked human samples (n=19) spanning the range of 0.3 to 11 mg/dL. The comparison was performed on the EPOS 5060 analyzer and gave the following results $y=1.02x-0.01$ mg/dL, $r=0.999$.

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:

Direct Bilirubin - Adult/elderly/child 0.1 - 0.3 mg/dL as recommended in Mosby's Diagnostic and Laboratory Test Reference, Mosby, St.Louis, Mo,1995,pp.108

Total Bilirubin - Adult/elderly/child 0.1 - 1.0 mg/dL as recommended in Mosby's Diagnostic and Laboratory Test Reference, Mosby, St.Louis, Mo,1995,pp.108

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.