

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

A. 510(k) Number:

k053090

B. Purpose for Submission:

New device

C. Measurand:

Bilirubin

D. Type of Test:

Quantitative, Enzymatic

E. Applicant:

Beckman Coulter, Inc.

F. Proprietary and Established Names:

Beckman Coulter Dri-STAT® Enzymatic Bilirubin Reagent

G. Regulatory Information:

1. Regulation section:

21 CFR §862.1110, Bilirubin (total and direct) test system

2. Classification:

Class II

3. Product code:

JFM

4. Panel:

75, Chemistry

H. Intended Use:

1. Intended use(s):

Dri-STAT® Enzymatic Bilirubin Reagent, in conjunction with the Synchron® Systems Bilirubin Calibrator, is intended for use in the in vitro diagnostic determination of total bilirubin in human serum and plasma as a User Defined Reagent (UDR) application on SYNCHRON® Systems.

2. Indication(s) for use:

Dri-STAT® Enzymatic Bilirubin Reagent, in conjunction with the Synchron® Systems Bilirubin Calibrator, is intended for use in the in vitro diagnostic determination of total bilirubin in human serum and plasma as a User Defined Reagent (UDR) application on SYNCHRON® Systems.

Measurements of total bilirubin in serum and plasma are used in the diagnosis of hemolytic disorder, biliary obstruction, hepatitis and cirrhosis.

3. Special conditions for use statement(s):

This product is for prescription use only

4. Special instrument requirements:

Beckman Coulter Synchron LX and CX System(s)

I. Device Description:

The device kit contains 3 x 3 mL bottles of the enzyme reagent which is reconstituted with 3 mL of deionized water into each bottle and one bottle of buffer which is ready to use. The reagent is transferred manually into a Beckman Coulter User-Defined Cartridge. The calibrators and controls are sold separately. The controls were previously cleared under k013235, k003488 and k001458. The calibrator was previously cleared under k791141

Human source material was tested and found negative for HIV 1 and 2, HBV and HCV using FDA approved methods.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dri-STAT Enzymatic Bilirubin Reagent on Cobas Fara

Synchron Systems Bilirubin Calibrator

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

k843174 and k791141, respectively

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Dri-STAT® Enzymatic Bilirubin Reagent, in conjunction with the Synchron® Systems Bilirubin Calibrator, is intended for use in the in vitro diagnostic determination of total bilirubin in human serum and plasma as a User Defined Reagent (UDR) application on SYNCHRON® Systems.	Same
Methodology	Enzymatic	Enzymatic
Reactive Ingredients	Bilirubin oxidase 25,000 U/l, Buffer Tris (hydroxymethyl) amino methane 100 mmol/L	Same
Sample Types	Serum and plasma	Same
Calibrator	Synchron Systems Bilirubin Calibrator	Same

Differences		
Item	Device	Predicate
Instrument Platforms	Synchron Systems LX & CX	Cobas Fara
Reference Intervals	0.3 -1.2 mg/dL	0.1 – 1.0 mg/dL
Wavelength	470 and 520 nm	465 nm
Reaction volumes	10, 200 and 16 µL	0.05, 1.00 and 0.08 mL

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

Area of Study	Reference Procedure	Reference Title
Method Comparison	CLSI/NCCLS EP9-A	User Comparison of Quantitative Clinical Laboratory Methods Using Patient Samples
Precision	CLSI/NCCLS EP5-A	User Evaluation of Precision Performance of Clinical Chemistry Devices
Linearity	CLSI/NCCLS EP6-A	Evaluation of the Linearity of Quantitative Methods
Traceability	prEN ISO 17511	In vitro diagnostic medical devices—Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and control materials
Interferences	CLSI/NCCLS EP7-A	Interference Testing in Clinical Chemistry
Reference Interval	CLSI/NCCLS C28-A2	How to Define and Determine Reference Intervals in the Clinical Laboratory

L. Test Principle:

The Dri-STAT® Enzymatic Bilirubin Reagent employs an enzymatic method, in which bilirubin oxidase catalyses the oxidation of bilirubin and produces a loss in the characteristic yellow absorption band. In the assay medium provided, total bilirubin is determined by measuring the decrease in absorbance at 479 nm and 520 nm. The total absorption change is proportional to the concentration of bilirubin in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Imprecision was assessed by three control samples and one serum pool. Four randomized runs were performed five times over twenty days. Each run contained two replicates. Acceptance criteria is a SD of <0.15 for the within run and a SD <0.225 for the total imprecision. The results are presented in the table below:

Sample	Number	Mean (mg/dL)	SD (mg/dL)	%CV
Within-Run Imprecision				
Serum Control 1	80	0.7	0.03	4.8
Serum Control 2	80	4.0	0.05	1.1
Serum Control 3	80	7.3	0.08	1.1
Human Pool	80	19.7	0.12	0.6
Total Imprecision				
Serum Control 1	80	0.7	0.03	4.8
Serum Control 2	80	4.0	0.06	1.4
Serum Control 3	80	7.3	0.11	1.5
Human Pool	80	19.7	0.47	2.4

b. *Linearity/assay reportable range:*

The linearity of the bilirubin measurement was demonstrated by taking a pooled serum sample and splitting into two samples. One sample is spiked with purified bilirubin to a concentration of 25 mg/dL. The two samples were inter-diluted to make a total of seven levels spanning the range of the assay 0-25 mg/dL. Each sample was tested in triplicate and the average recovery was calculated and plotted against the targeted recoveries. Linear regression of comparison data yielded the following relationship:

$$y = 1.002x - 0.007, r = 1$$

The reportable range for bilirubin measurements is 0.2-25 mg/dL

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

The calibrators were previously cleared under k791141. The traceability process is based on prEN ISO 17511.

The configuration and formulation of the bilirubin reagent is the same as the predicate, therefore the shelf life stability of the assay was determined in the predicate submission k843174 and not repeated for this submission.

On-board stability was determined by calibrating the instrument and running controls solutions. The controls were periodically run over 18 days and the values were compared to the original values. Acceptance criterion is ± 1.3 times the within run Imprecision SD (0.15 mg/dL) or CV% (3%). On-board stability demonstrated acceptable stability of 14-days.

d. *Detection limit:*

The analytical sensitivity of the assay was evaluated by testing 20 replicates of saline (zero) and a patient sample diluted (with saline) to achieve a concentration less than the claimed sensitivity. Assay sensitivity is distinguishable with 95% confidence ± 2 SD. The analytical sensitivity of the assay is 0.2 mg/dL.

The functional sensitivity is defined as the lowest bilirubin concentration determined at a CV of less than 20%. The functional sensitivity was determined to be 0.2 mg/dL

e. *Analytical specificity:*

Studies were performed to assess common or known substances that could interfere with the method. A substance was considered to show no significant interference if the test sample was within 0.3 mg/dL or 6% of the control specimen recovery. A summary of the data for know interferences appears for the common interferences in the table below:

Interferent	Source	Level of Interferent	Bilirubin Level (mg/dL)	Observed effect (mg/dL)
Hemoglobin	RBC hemolysate	250 mg/dL	0.2	NSI
			7.5	± 0.7
			15	± 1.1
Lipemia	Intralipid	250 mg/dL	0.2	± 0.3
			7.5	NSI
			15	NSI

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

Clinical correlation studies were performed comparing the Dri-STAT Enzymatic Bilirubin reagent results on the Synchron LX and CX systems against the results from the Cobas Fara using serum samples. The correlations are as follows:

LX Platform – $y = 1.031x + 0.016$, $r = 0.9997$, $n = 70$

CX Platform – $y = 1.004x + 0.004$, $r = 0.9997$, $n = 70$

b. *Matrix comparison:*

A serum and plasma comparison study was conducted to substantiate the use of EDTA anticoagulant for bilirubin testing. Paired samples were analyzed by the assay on the Synchron Systems. The correlation was as follows:

$y = 0.952x - 0.038$, $r = 0.999$, $n=58$

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:

The following reference range was obtained from the literature and verified by drawing blood from 20 apparently non-smoking healthy adults. All samples were run in duplicate. The acceptance criteria required at least 90 % of the samples to have bilirubin values within the cited reference interval. The reference range was determined to be 0.3 – 1.2 mg.dL.

Tietz, N.W., ed., Textbook of Clinical Chemistry, Third Edition, W.B Saunders, Philadelphia, PA (1999)

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.