

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

A. 510(k) Number:

k063845

B. Purpose for Submission:

New Device

C. Measurand:

Bilirubin

D. Type of Test:

Quantitative Colorimetric assay

E. Applicant:

Bayer Healthcare, LLC

F. Proprietary and Established Names:

Advia Chemistry Total Bilirubin 2

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 indications for use below.

2. Indication(s) for use:

For in vitro diagnostic use in the quantitative determination of total bilirubin in human serum and plasma on the ADVIA Chemistry Systems. Such measurements are used in the diagnosis and treatment of hemolytic, biliary, and liver disorders, including hepatitis and cirrhosis.

3. Special conditions for use statement(s):

For prescription use only. Not intended for use with neonates.

4. Special instrument requirements:

ADVIA Chemistry System

I. Device Description:

The device consists of two ready to use reagents. Both reagents contain buffers and/or stabilizers. Calibrators were previously cleared under k030169 and controls under k883209.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ADVIA IMS Total Bilirubin Assay

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

k992399

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Specimen Type	Human serum or plasma (lithium heparin)	Human serum or plasma (lithium heparin)
Reaction Type	Colorimetric endpoint	Colorimetric endpoint
Calibration	Single point	Single point

Differences		
Item	Device	Predicate
Principle	Vanadate oxidation	Diazotized sulfanic acid with blank
Reagents	Two liquid reagents contained in system specific packaging	One lyophilized reagent, diluent, and one liquid reagent contained in system specific packaging
Measuring range	0.1 – 35 mg/dL	0 – 40 mg/dL
Intended use	For the quantitative determination of total bilirubin in adults	For the quantitative determination of total bilirubin

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

CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods

CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation

L. Test Principle:

The Total Bilirubin 2 assay is based on a vanadate oxidation method. Total bilirubin (conjugated and unconjugated) is oxidized by vanadate at about pH 2.9 to produce biliverdin. In the presence of detergent and vanadate, both conjugated and unconjugated bilirubin are oxidized. The oxidation reaction causes a decrease in the optical density which is proportional to the total bilirubin concentration in the sample. The concentration is measured as an endpoint reaction.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within run and total imprecision were evaluated on each chemistry platform by testing five levels of serum pools. Each sample was assayed two times per run, 1 or 2 runs per day for at least 10 days. Precision estimates were computed according to CLSI EP5-A2, Evaluation of Precision Performance of Quantitative Measurement Methods. The results are summarized below.

ADVIA 1200 Precision

Specimen Type	Level mg/dL	Within-run		Total	
		SD	CV%	SD	CV%
Serum	1.1	0.00	0.4	0.04	3.6
Serum	7.6	0.02	0.3	0.10	1.3
Serum	14.7	0.08	0.5	0.21	1.4
Serum	22.1	0.16	0.7	0.32	1.4
Serum	27.6	0.32	1.2	0.47	1.7

ADVIA 1650/1800 Precision

Specimen Type	Level mg/dL	Within-run		Total	
		SD	CV%	SD	CV%
Serum	1.0	0.01	1.3	0.02	2.0
Serum	7.1	0.15	2.2	0.19	2.6
Serum	15.4	0.06	0.4	0.49	3.2
Serum	22.1	0.11	0.5	0.26	1.2
Serum	27.5	0.14	0.5	0.30	1.1

ADVIA 2400 Precision

Specimen Type	Level mg/dL	Within-run		Total	
		SD	CV%	SD	CV%
Serum	1.0	0.05	4.6	0.05	4.7
Serum	7.2	0.15	2.0	0.16	2.3
Serum	15.5	0.12	0.8	0.25	1.6
Serum	21.8	0.09	0.4	0.21	1.0
Serum	27.1	0.30	1.1	0.41	1.5

b. Linearity/assay reportable range:

Nine equally spaced levels of serum pools prepared using high and low linearity pools were tested on the ADVIA 1200, 1650, and 2400 platforms. The sample concentrations tested ranged from approximately 0.17 mg/dL to 37.5 mg/dL. All results were within $\pm 5\%$ of the expected value except the lowest dilution level which had concentrations approaching the limits of detection of the assay. The results of the lowest dilution level were all with \pm

0.03 mg/dL of the expected value. The reportable range for all platforms is 0.1 mg/dL to 35 mg/dL.

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

The sponsor states that the calibrators are traceable to the AACC reference method, which used reference materials from NIST, via patient correlation.

Protocols and acceptance criteria were reviewed for reagent stability. The reagents are stable until their expiration dates when stored as instructed. Calibrators were previously cleared under k030169 and controls under k883209.

d. Detection limit:

The limit of detection and the limit of the blank were determined as outlined in CLSI EP17-A. A blank sample (saline) was evaluated 64 times on each platform to calculate the limit of the blank. A low level sample was also run 64 times on each platform and used to calculate the limit of detection. The observed limits of detection on the three platforms were all below the claimed low end of the measuring range of the assay (0.1 mg/dL).

e. Analytical specificity:

The interference study was carried out in the presence of approximately 1 mg/dL and 20 mg/dL total bilirubin. The samples were evaluated on the ADVIA 1200, 1650, and 2400. All samples were evaluated in duplicate with multiple concentrations of each interferant. Lack of interference was defined as a bias of <10% compared to a sample without the interfering substance present. The assay showed no interference with up to 50 mg/dL ascorbic acid, 1000 mg/dL hemoglobin, and 1000 mg/dL triglycerides.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Correlation studies were performed by first comparing adult patient samples on the ADVIA 1650 to the ADVIA IMS predicate device. The same adult patient samples were then measured on the ADVIA 1200 and ADVIA 2400 and compared to the ADVIA 1650. The studies were performed over 5 days and the results are summarized below.

Specimen	System	Comparison system	N	Regression equation	r
Serum	ADVIA 1650	ADVIA IMS	118	$Y=0.925x+0.12$	0.998
Serum	ADVIA 1200	ADVIA 1650	119	$Y=1.036x-0.05$	1.000
Serum	ADVIA 2400	ADVIA 1650	119	$Y=0.999x-0.02$	1.000

b. *Matrix comparison:*

The serum/plasma equivalence study was carried out using lithium heparin plasma samples and the corresponding serum samples drawn from volunteers. Samples were spiked with unconjugated bilirubin in order to cover the measuring range. The samples, ranging from 0.3 mg/dL to 34.4 mg/dL, were run on all three platforms and the results are shown below.

Platform	N	Regression equation	r
ADVIA 1200	49	$Y=1.012x-0.00$	1.000
ADVIA 1650	58	$Y=1.019x-0.02$	0.999
ADVIA 2400	57	$Y=1.012x+0.01$	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

1. Expected values/Reference range:

Expected values from Tietz NW. Clinical Guide to Laboratory Tests. 3rd ed. Philadelphia, PA WB Saunders Company; 1995: 88-91

	mg/dL
Adult	0.2 – 1.2

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.