

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

A. 510(k) Number:

k053132

B. Purpose for Submission:

New Device

C. Measurand:

Bilirubin, Direct

D. Type of Test:

Enzymatic Colorimetric

E. Applicant:

Wako Chemicals USA, Inc.

F. Proprietary and Established Names:

Wako Direct Bilirubin V

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:

Determination of serum and plasma bilirubin is useful in the screening of liver function disorders or in the diagnosis of jaundice.

3. Special conditions for use statement(s):

For prescription use only.

This assay has not been tested in neonates.

4. Special instrument requirements:

ADVIA 1650 Analyzer

I. Device Description:

The Wako Direct Bilirubin V is a dual reagent system. Both reagents contain stabilizers and/or buffers. To calibrate the test kit, a previously cleared calibrator is used that has values determined by a similar method.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Wako Direct Bilirubin V

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

k970986

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Method	Colorimetric	Colorimetric
Linearity	0.1 to 20 mg/dL	0.1 to 20 mg/dL

Differences		
Item	Device	Predicate

Differences		
Item	Device	Predicate
Storage Temp.	2 -10° C	2 -35° C
Matrix	Serum and Plasma	Serum

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

CLSI EP5-T2 Evaluation of Precision Performance of Clinical Chemistry Devices

CLSI Protocol EP9-A Method Comparison and Bias Estimation Using Patient Samples

CLSI Protocol EP6-A Evaluation of the Linearity of Quantitative Analytical Methods; Approved Guideline

CLSI EP7-P Interference Testing in Clinical Chemistry; Approved Guideline- Second Edition

L. Test Principle:

The Wako Direct Bilirubin V uses an enzymatic method for bilirubin detection. Direct bilirubin reacts with vanadate under acidic conditions, and is oxidized to biliverdin. The resulting absorbance change is colorimetrically measured at 451 nm.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

All studies were conducted on the ADVIA 1650 analyzer unless stated otherwise.

a. *Precision/Reproducibility:*

Within-run precision was conducted with Wako Direct Bilirubin V with 22 or 23 replicates of five sample concentrations.

	Replicate	Mean (mg/dL)	S.D.	C.V. (%)
Sample 1	23	0.3	0.01	1.87
Sample 2	23	1.5	0.02	1.11
Sample 3	22	1.3	0.03	2.37
Sample 4	22	9.9	0.07	0.73
Sample 5	22	19.9	0.16	0.83

Total precision was conducted on two levels of pooled sera, in the abnormal and normal ranges. Samples were run in duplicate for 20 days.

Level	# of days	Mean	S.D.	C.V. (%)
-------	-----------	------	------	----------

		(mg/dL)		
Low	20	0.4	0.013	3.51
High	20	0.7	0.24	3.75

An accuracy study was conducted with the Wako Direct Bilirubin V by running 6 human serum samples in replicates of 5.

	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Sample 6
Added (mg/dL)	0	1.1	3.6	7.6	14.6	18.6
Expected (mg/dL)	1.4	2.5	5.0	9.0	16.0	20.0
Observed mean (mg/dL)	1.4	2.48	4.92	8.88	16.3	20.1
Recovery %	100%	99%	98%	99%	102%	101%

b. Linearity/assay reportable range:

A dilution linearity study was conducted and the sponsor claims a linear range of 0.1 to 20 mg/dL. The labeling informs user that if the direct bilirubin concentration exceeds 20 mg/dL, a 1:1 sample dilution with saline is required and the result is multiplied by 2. Seventy two plasma and serum pairs that ranged from 0.07 to 22.17 mg/dL were analyzed and the linear regression equation was reported as $y=0.985x + 0.055$ and $r=0.999$.

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

The Wako Direct Bilirubin is stable when stored at 2 to 10° C until its expiration date.

d. Detection limit:

The minimum level of detection is 0.1 mg/dL and was calculated by running a known zero sample (water) for 21 replicates. The mean plus 2 SD was used to calculate the minimum level of detection of 0.1 mg/dL.

e. Analytical specificity:

No interference was observed by ascorbic acid up to 50 mg/dL, hemoglobin up to 500 mg/dL and Intrafat up to 2%. Anticoagulants were also studied and no interference was detected with EDTA, citrate, oxalate, sodium flouride and heparin.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

The Wako Direct Bilirubin V was compared to the Wako 30R Bilirubin V that was previously cleared in 1991. A comparison of bilirubin measurements by the current device (y) and the predicate device (x) was performed using 84 serum samples. The equation of $y = 0.971x + 0.020$ with a $r = 0.912$ was obtained with using the Hitachi 911.

b. *Matrix comparison:*

A comparison of 36 matched serum and plasma samples (31 patient samples and 5 spiked samples run in duplicate) that ranged from 0.07 to 22.2 mg/dL was performed. Of the 36 matched serum and plasma samples, 5 were spiked with a concentrated form of human bilirubin calibrator to evaluate the comparison at the high end of the linear range. The 31 patient samples were drawn fresh daily and run in duplicates for 7 days. The comparison was performed on the ADVIA 1650 analyzer and gave a correlation coefficient of $r = 0.9989$ and a regression equation of $y = 0.985x + 0.05$.

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:

The sponsor states that the expected value of direct bilirubin in serum and plasma is 0.0 – 0.2 mg/dL as recommended in Tietz Textbook of Clinical Chemistry by Carl A. Burtis and Edward R. Ashwood.

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.