

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k061830

B. Purpose for Submission:

Addition of the detection of total bilirubin to the Nova Stat Profile Clinical Care Xpress (CCX) System.

C. Measurand:

Bilirubin, Total

D. Type of Test:

Quantitative Absorbance Assay

E. Applicant:

Nova Biomedical Corporation

F. Proprietary and Established Names:

Nova Stat Profile Clinical Care Xpress (CCX 1+) System

G. Regulatory Information:

1. Regulation section:

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

21 CFR § 862.1150, Calibrator, Secondary Control

21 CFR § 862.1660, Quality control material (assayed and unassayed)

2. Classification:

Class II (Assay)

Class II (Calibrator)

Class I, reserved (General Controls)

3. Product code:

CIG, diazo colorimetry, bilirubin

JIT, calibrator, secondary

JJY, multi-analyte controls, all kinds (assayed and unassayed)

4. Panel:

75 (Clinical Chemistry)

H. Intended Use:

1. Intended use(s):

See Indications for use.

2. Indication(s) for use:

The Stat Profile Critical Care Xpress Analyzer is intended for *in vitro* diagnostic use by health care professionals and for point-of-care usage in the quantitative determination of pH, PCO₂, PO₂, SO₂%, Hematocrit (Hct), total Hemoglobin (tHb), Oxyhemoglobin (O₂Hb), Carboxyhemoglobin (COhb), Methemoglobin (MetHb), Reduced Hemoglobin (HHb), Oxygen content (O₂Ct), Oxygen capacity (O₂Cap), and total Bilirubin (tBil) in heparinized whole blood; Na⁺, K⁺, Cl⁻, Ca⁺⁺, Mg⁺⁺, Glucose (Glu), Lactate (Lac), BUN (Urea), and Creatinine (Creat) in heparinized whole blood, serum, or plasma. Total Bilirubin (tBil) was not evaluated on neonatal samples.

The intended use of the Nova Stat Profile Critical Care Xpress CO-Oximeter Calibration Cartridge with Bilirubin and Deproteinizing Solution is for the quantitative determination of total hemoglobin, oxyhemoglobin, carboxyhemoglobin, methemoglobin, deoxyhemoglobin and total bilirubin in human blood using the Nova Stat Profile Critical Care Xpress Analyzer.

Nova Stat Profile Critical Care Xpress CO-Oximeter Controls and Auto cartridge QC are intended for *in vitro* diagnostic use by healthcare professionals for monitoring the performance of Nova Biomedical Stat Profile Critical Care Xpress Analyzers.

3. Special conditions for use statement(s):
For prescription use. Not for use on neonates.
4. Special instrument requirements:
Nova Stat Profile Clinical Care Xpress (CCX 1+) System

I. Device Description:

The Nova Stat Profile Clinical Care Xpress System was previously cleared under 510(k)s k020297 and k022746. The current submission (k061830) is for the addition of total bilirubin to the analytes measured by the instrument. Total Bilirubin is an *in vitro* diagnostic assay for the quantitative determination of total bilirubin in human heparinized whole blood. The calibrators or controls that are available are traceable to NIST Standard Reference Material 916A Bilirubin.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Dade Dimension RXL, Radiometer ABL 800 Flex
2. Predicate 510(k) number(s):
k840777 and k050869 respectively.
3. Comparison with predicate:

Comparison			
Item	Device	Predicate (Dimension RXL)	Predicate (ABL 800 Flex)
Analyte	Total Bilirubin	Total Bilirubin	Total Bilirubin
Operating Principle	Spectrophotometry, Direct	Spectrophotometry, Indirect	Spectrophotometry, Direct
Measuring Range	0.5-35.1 mg/dL	0-25 mg/dL	0-23.4 mg/dL test range 0-58.5 mg/dL measuring range
Sample Size	110 µL	65 µL	85 µL
Cycle Time	100 seconds	12 minutes	145 seconds
Calibration	Automatic for total hemoglobin/bilirubin	Manual for total bilirubin	Manual for total hemoglobin
Analyzer Type	Bench top	Floor model	Bench top
Calibrators	One level	Three levels	One level
Controls	Three levels	Three levels	Four levels

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

None identified.

L. Test Principle:

The sample collection, preparation, and application to the analyzer is the same as for the previously cleared CCX model. The existing spectrophotometer in the analyzer is used to measure total bilirubin directly at a specific wavelength accomplished through the addition of a new algorithm in the instrument software.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Within-run precision was determined by measuring twenty (20) replicates of a given sample on two different analyzers. The samples analyzed were NOVA CO-Oximeter Controls Levels 7 (3.4 - 4.6 mg/dL), 8 (8.8 - 11.2 mg/dL), 9 (17.6 – 22.4 mg/dL) and whole blood. Heparinized whole blood was analyzed twenty (20) consecutive times on the STP CCX1+ CO-Oximeter. The whole blood samples were modified to yield bilirubin concentrations of 1 mg/dL and 12 mg/dL. Results are summarized below.

Control Level 7 Within Run Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	20	4.2	0.04	0.87
2	Total Bilirubin	20	4.0	0.05	1.30

Control Level 8 Within Run Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	20	10.1	0.15	1.53
2	Total Bilirubin	20	9.8	0.14	1.42

Control Level 9 Within Run Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	20	19.5	0.19	0.97
2	Total Bilirubin	20	19.8	0.09	0.48

Whole Blood Within Run Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	20	1.2	0.07	6.69
2	Total Bilirubin	20	1.0	0.09	8.81
1	Total Bilirubin	20	12.7	0.36	2.84
2	Total Bilirubin	20	12.1	0.40	3.33

Day to Day precision was determined by triplicate measurements of a given sample on each of 20 test runs over 20 days. The samples analyzed were the NOVA CO-Oximeter Controls Levels 7, 8, and 9. Results are summarized below.

Control Level 7 Day to Day Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	60	4.2	0.08	1.82
2	Total Bilirubin	60	4.0	0.08	1.93

Control Level 8 Day to Day Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	60	10.1	0.16	1.60
2	Total Bilirubin	60	10.0	0.19	1.87

Control Level 9 Day to Day Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	60	20.1	0.30	1.52
2	Total Bilirubin	60	20.0	0.30	1.52

Precision of the STP CCX1 + COOX in the high end of the claimed total bilirubin reference range (0.2 to 1.0 mg/dL) was determined by measuring day to day precision of a bilirubin concentration of 1.0 mg/dL. The day to day precision was determined by analyzing triplicate measurements of these samples in 20 runs over 10 days on two instruments. Results are summarized below.

Normal Level Day to Day Precision

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	Total Bilirubin	60	1.1	0.05	4.78
2	Total Bilirubin	60	1.0	0.07	6.53

b. *Linearity/assay reportable range:*

The measuring range of the device (0.5 to 35.1 mg/dL) was evaluated by comparing the two modes of the device, COOX only mode (using a 115 µL sample volume) and COOX with ABG mode (using a 210 µL sample volume). Of the 80 samples, seven samples ranging from 0.1 to 0.7 mg/dL were clinical samples and the remaining samples spanning from 2.3 to 35.0 mg/dL were spiked whole blood samples. The two studies are summarized below:

A single analysis of heparinized whole blood from healthy volunteers was processed on the STP CCX1+ CO-OXIMETER (COOX only mode) and compared to a single analysis on the Dade Dimension RxL. Total bilirubin level in heparinized blood was manipulated by spiking with bilirubin stock solution to obtain samples in the range of 0.5 mg/dL – 35.0 mg/dL. Eighty (80) samples were analyzed in a randomized fashion. A least squares regression analysis of the data was performed to assess system performance. Results are summarized below.

STP CCX1+ CO-OXIMETER ONLY ANALYSIS
versus Dade Dimension RxL:

Unit	Analyte	n	r ²	Slope	Y-Intercept
1	tBil	80	0.989	1.022	0.146
2	tBil	80	0.989	1.014	0.057

A single analysis of heparinized whole blood from healthy volunteers was processed on the STP CCX CO-OXIMETER as a combined analysis (COOX with ABG mode) and compared to a single analysis on the STP CCX1+ CO-OXIMETER (COOX only mode). Total bilirubin level in heparinized blood was manipulated by spiking with bilirubin stock solution to obtain samples in the range of 0.5 mg/dL – 35.0 mg/dL. A least squares regression analysis of the data was performed to assess system performance. Results are summarized below.

STP CCX1+ CO-OXIMETER AGB with COOX
versus the COMBINED ANALYSIS:

Unit	Analyte	n	r ²	Slope	Y-Intercept
1	tBil	80	0.989	1.007	0.067
2	tBil	80	0.988	1.004	0.220

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
 The calibrators and controls are traceable to NIST Standard Reference Material 916A Bilirubin. Stability characteristics of the controls and calibrators were determined using real time studies. The data submitted supports an open vial stability of 35 days and an unopened vial stability of 2 years at room temperature for both the controls and calibrator.

d. *Detection limit:*
 The lower limit of detection for total bilirubin was determined by measuring day to day imprecision of a solution containing ~0.4 mg/dL bilirubin which is below the low end of the analyzer’s measurement range of 0.5 – 35.1 mg/dL. Results are summarized below.

Unit	Analyte	n	Mean (mg/dL)	SD	CV (%)
1	tBil	60	0.4	0.08	19.19
2	tBil	60	0.3	0.10	32.42

e. *Analytical specificity:*
 Investigation of interference effects to total bilirubin measurements on the Nova CCX1+ CO-Oximeter was performed using high levels of potential interfering substances including: Lipids, Evans Blue, Indocyanine Green, Methylene Blue and EDTA. Samples spiked with all potentially interfering substances were within +/- 1.0 mg/dL of the reference instrument for all substances except 3% Lipid and 15mg/L Methylene Blue which showed biases of >1.0mg/dL. These substances (3% Lipid and 15mg/L Methylene Blue) are identified as interfering substances in the operator’s manual. The results are summarized below as the averages of three replicates.

Whole Blood ~7.0 mg/dl bilirubin spiked with various potential interfering substances	CCX1+ (mg/dL)	DADE (mg/dL)	Bias vs. Dade (mg/dL)
Blood (Control)	7.0	6.5	0.5
Lipid (3%)	4.8	6.2	-1.4
Lipid (1%)	5.6	6.5	-0.9
Lipid (0.5%)	6.2	6.8	-0.6
Evans Blue (5 mg/L)	6.0	6.2	-0.2
Methylene Blue (15 mg/L)	4.9	6.2	-1.3
Patent Blue (10 mg/L)	6.4	6.3	0.1
Indocyanine Green (5 mg/L)	6.6	5.9	0.7
EDTA (15 %)	7.0	6.4	0.6

Potential hemoglobin interference was also tested by modifying heparinized whole blood. For each of three levels of tHb, the total bilirubin concentration was manipulated by spiking with a bilirubin stock solution. A single analysis of each sample was processed on the STP CCX1 +

CO-Oximeter and compared to a single analysis on the Dade Dimension RxL. The sponsor defined interference non-interference as the total bilirubin value being within +/- 1.0 mg/dL or 10% of the reference instrument.

tHb	CCX tHb (g/dL)	CCX tBil (mg/dL)	Dade RxL tBil (mg/dL)	CCX Bias vs. Dade (mg/dL)	CCX % Diff. Vs. Dade
Low tHb	5.2	3.5	3.1	0.4	11.76
	6.9	4.3	4.7	-0.4	-8.56
	7.1	17.1	17.4	-0.3	-1.44
	9.8	0.6	0.6	0.0	1.82
	7.7	6.7	6.9	-0.2	-2.70
Normal tHb	14.1	0.5	0.6	-0.1	-15.31
	14.1	4.1	9.7	0.4	10.62
	16.1	17.7	17.0	0.7	4.26
	17.0	10.7	11.2	-0.5	-4.65
	17.2	18.6	18.1	0.5	2.83
High tHb	22.6	31.8	33.5	-1.7	-4.98
	22.6	2.0	1.8	0.2	9.50
	22.9	4.2	4.2	0.0	-0.48
	21.6	20.4	19.6	0.8	3.85
	22.6	10.6	9.8	0.8	8.53

f. Assay cut-off:
Not Applicable.

2. Comparison studies:

a. *Method comparison with predicate device:*

Un-spiked samples obtained from hospital patients were processed on the STP CCX1 + CO-Oximeter (COOX only mode) using two instruments and compared to a single analysis on the Dade Dimension RxL. A total of 68 samples were analyzed and a least squares regression analysis of the data was performed to assess system performance. Results are summarized below:

Instrument	Analyte	n	r ²	Slope	y-intercept	Min	Max
1	tBil	62	0.9849	1.017	0.116	0.5	32.5
2	tBil	62	0.9867	1.013	0.089	0.6	32.8

b. *Matrix comparison:*

See above: *Method comparison with predicate device*

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):*

A Point of Care study was performed at a single site using 110 individuals (55 hospital personnel, 50 Point of Care (POC) personnel, and 5 laboratory personnel). Performance of the device was evaluated by comparing results from 88 clinical samples spanning a total bilirubin range from 0.5 to 33.5 mg/dL performed by both hospital personnel and non-hospital personnel. Results of the comparison are summarized below:

Analyte	n	r ²	Slope	Y-Intercept
Total Bilirubin	88	0.998	1.007	0.044

Precision was also evaluated by POC personnel using the same control levels as in the Precision/Reproducibility section above. Results are summarized below.

Control Level 7 Run to Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	4.7	0.05	1.01

Control Level 8 Run to Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	9.98	0.04	0.41

Control Level 9 Run to Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	20.3	0.23	1.16

Control Level 7 Within Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	4.7	0.05	1.01

Control Level 8 Within Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	10.2	0.06	0.58

Control Level 9 Within Run Precision

Analyte	n	Mean (mg/dL)	SD	CV (%)
Total Bilirubin	20	20.5	0.099	0.48

4. Clinical cut-off:
Not Applicable.

5. Expected values/Reference range:

The sponsor included the following reference values for normal total bilirubin levels in the operator's manual:

Total Bilirubin (tBil) Adult: 0.2 – 1.0 mg/dL

From: The reference value for total bilirubin was obtained from Tietz, Norbert W., ed. 1983. Clinical Guide to Laboratory Tests. Philadelphia, PA: W.B. Saunders Co.

N. Instrument Name:

Nova Stat Profile Clinical Care Xpress (CCX 1+) System

O. System Descriptions:

1. Modes of Operation:

The instrument has several modes of operation for the various analytes and sample types (whole blood, serum, and plasma). For total bilirubin, the instrument can use only the whole blood sample type.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes or No

3. Specimen Identification:

Sample identification is performed through an interface which instructs the device which sample type is to be detected.

4. Specimen Sampling and Handling:

The sponsor indicates in the operator's manual that correct handling is critical to ensure that the blood gas values obtained accurately reflect the *in vivo* state. It is recommended that the samples be well mixed prior to introduction into the analyzer and that the samples be analyzed within 15 minutes for blood gases. The sponsor references CLSI document C32-P. Vol. 13, No. 17. Considerations in the Simultaneous Measurement of Blood Gases, Electrolytes, and Related Analytes in Whole Blood: Proposed Guideline.

5. Calibration:

The instrument has a two-point and single-point automatic calibration for total bilirubin. The same dye reagents (cleared in k022746) are used for the measurement of total bilirubin and there is no change to the formulation of the calibrators as a result of the added analyte measurement.

6. Quality Control:

The sponsor provides several levels of controls for use with the instrument and QC procedures are listed in the operator's manual. An acceptable range for each control level is printed on the control solution label and the user is referred to the troubleshooting section of the operator's manual if control results fall outside these ranges. The same reagents dyes (cleared in k022746) are used for the measurement of total bilirubin and there is no change to the formulation of the controls as a result of the added analyte

measurement.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The “Performance Characteristics” Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

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