510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K251998

B Applicant

Siemens Healthcare Diagnostics Inc.

C Proprietary and Established Names

Atellica CH Diazo Total Bilirubin (D_TBil)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
CIG	Class II	21 CFR 862.1110 - Bilirubin (total or direct) test system	CH - Clinical Chemistry
MQM	Class I, reserved	21 CFR 862.1113 - Bilirubin (total and unbound) in the neonate test system	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

Modified device

B Measurand:

Total Bilirubin

C Type of Test:

Quantitative, photometric test

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Atellica CH Diazo Total Bilirubin (D_TBil) assay is for in vitro diagnostic use in the quantitative determination of of total bilirubin in human serum and plasma of adults and neonates using the Atellica CH Analyzer. Measurement of total bilirubin, an organic compound formed during the normal and abnormal destruction of red blood cells, is used in the diagnosis and treatment of liver, hemolytic, hematological, and metabolic disorders, including hepatitis and gallbladder block. A total bilirubin measurement in newborn infants is intended to aid in indicating the risk of bilirubin encephalopathy (kernicterus).

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Atellica CH Analyzer

IV Device/System Characteristics:

A Device Description:

The Atellica CH Diazo Total Bilirubin (D_TBil) assay consists of the following 2 packs:

Pack 1 (P1)	23.5 mL	Phosphate buffer (50mmol/L); NaCl (150mmol/L)
Pack 2 (P2)	8.8ml	2,4-Dicholoroaniline (5mmol/L); HCl (130mmol/L); Na-Nitrite (0.5mmol/L)

Materials required but not provided: Atellica CH Bilirubin Calibrator (BILI CAL)

B Principle of Operation:

The Atellica CH Diazo Total Bilirubin (D_TBil) is an assay that uses 2,4-dichloroaniline (DCA). Direct bilirubin in the presence of diazotized DCA forms a red-colored azocompound in acidic solution that can be measured. A specific mixture of detergents enables the determination of total bilirubin. The detection wavelength is 545nm. This assay requires 6.0 µL of sample for a single determination.

V Substantial Equivalence Information:

A Predicate Device Name(s):
cobas c Bilirubin Total Gen.3

B Predicate 510(k) Number(s):
K131544

C Comparison with Predicate(s):

Device & Predicate Device(s):	K251998	K131544
Device Trade Name	Atellica CH Diazo Total Bilirubin (D_TBil)	Roche cobas c Total Bilirubin Gen. 3
General Device Characteristic Similarities		
Intended Use/Indications For Use	Quantitative determination of total bilirubin in human serum and plasma of adults and neonates.	Same
Measurand	Total Bilirubin	Same
General Device Characteristic Differences		
Measuring Range	0.10 mg/dL – 25.00 mg/dL	0.146 -35.1 mg/dL
Instrument Platform	Atellica CH Analyzer	Roche/Hitachi Cobas c 501 Analyzer
Sample Matrix	Human serum and plasma (lithium heparin, sodium heparin, dipotassium EDTA)	Human serum and plasma (lithium heparin, dipotassium EDTA)

VI Standards/Guidance Documents Referenced:

Clinical Laboratory Standards Institute (CLSI) EP07-3rd Edition – Interference Testing in Clinical Chemistry
CLSI EP09c 3rd Edition – Measurement Procedure Comparison and Bias Estimation Using Patient Samples
CLSI EP28-A3c (Formerly C28-A3c) – Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline –Third Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Precision for the Atellica CH Diazo Total Bilirubin (D_TBil) was previously established in K222104.

2. Linearity:

   Linearity for the Atellica CH Diazo Total Bilirubin (D_TBil) was previously established in K222104.

3. Analytical Specificity/Interference:

   Interference testing for the Atellica CH Diazo Total Bilirubin (D_TBil) was previously established in K222104.

   Interferences typically seen in samples from neonates, not already evaluated in K222104, were evaluated according to CLSI EP07 3rd Edition. The effect of fetal hemoglobin (HbF) on the D_TBil assay was evaluated using two human serum pools spiked to obtain bilirubin concentrations of ~1.0 mg/dL or ~14.0 mg/dL. Each sample was tested in 5 replicates. Testing used the paired-difference method of comparing a sample spiked with interferent to a sample spiked with control material (diluent used in the test sample). The sponsor considered interference to be non-significant if the difference between the samples with and without interferent are within 10.0%. The results of the interference study are summarized below.

Potentially Interfering Substance	Highest concentration of interferent tested that did not show significant interference
Fetal Hemoglobin	1000 mg/dL

4. Detection Limit and Assay Reportable Range:

   The detection limits for the Atellica CH Diazo Total Bilirubin (D_TBil) were previously established in K222104.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The assay is traceable to the SRM916 (NIST) Standard Reference Material.

6. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:
   A method comparison study was conducted in accordance with CLSI EP09c-A3 using 124 serum samples from neonates with ages of <1 day to 27 days. Samples were tested with one of three different reagent lots on one Atellica CH Analyzer. Results from the candidate device were compared to results from the predicate device. Data were analyzed using Passing-Bablok regression analysis. In the method comparison study, the 124 samples were in the range of 0.10 -21.81 mg/dL.

   The table below provides %Bias along with two-sided 95%CI at the Medical Decision Levels (MDLs):

MDL	%Bias	95%CI
1 mg/dL	0.0%	(-4.4%; 3.5%)
8 mg/dL	4.6%	(3.4%; 5.8%)
13 mg/dL	7.7%	(6.1%; 11.8%)
17 mg/dL	8.7%	(8.7%; 11.8%)

   Another method comparison study was performed on 41 serum samples from neonates with ages of <1 hour to <28 days. Results from the candidate device were compared to results from a legally marketed comparator method. Data were analyzed using Passing-Bablok regression analysis. In the method comparison study, 41 samples were in the range of 0.40 -11.40 mg/dL. The table below provides %Bias along with two-sided 95%CI at the Medical Decision Levels (MDLs):

MDL	%Bias	95%CI
1 mg/dL	0.4%	(-2.8%; 2.5%)
8 mg/dL	4.2%	(3.4%; 4.9%)

   The sponsor also demonstrated close alignment (i.e., negligible bias at MDLs) to a well-recognized and accepted reference method.

2. Matrix Comparison:

   Matrix equivalency between serum and plasma (lithium heparin, sodium heparin, dipotassium EDTA) was established in K222104.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off:

Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Expected Values/Reference Range:

The reference interval for the Atellica CH Diazo Total Bilirubin (D_TBil) is outlined in the literature reference: Wu AHB. Tietz Clinical Guide to Laboratory Tests, 4th edition, Saunders Elsevier, St. Louis, MO: 2006:172. Verification of the described reference range was completed in accordance with CLSI EP28-A3c with a minimum of 20 samples for each age category listed. Each age group was analyzed separately with data summarized in the table below. The reference range verification study supports the use of the literature reference interval.

Age Range	Acceptable Range
0-1 day	< 8.00 mg/dL
1-2 days	< 12.0 mg/dL
3-5 days	< 16.0 mg/dL
>5 days	0.30– 1.20 mg/dL

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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