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Performance Evaluation of the Atellica CH Total Bilirubin_2 Assay to Include Neonates*

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Background

The purpose of the investigation was to add neonatal claims to the Atellica® CH Total Bilirubin_2 (TBil_2) Assay and to evaluate the analytical performance of these claims on the Atellica CH Analyzer. Total bilirubin is formed by the breakdown of hemoglobin by the liver. In neonates, particularly those born prematurely, increased bilirubin is often due to the immature liver being unable to produce the enzyme glucuronosyltransferase, which assists in the breakdown of bilirubin. If bilirubin accumulates to toxic levels,the newborn is at risk for brain damage and other complications. The Atellica CH TBil_2 Assay uses vanadate to oxidize both conjugated (direct) and unconjugated bilirubin. This reaction causes a reduction in the optical density of the yellow color specific to bilirubin. The decrease in optical density is proportional to the concentration of total bilirubin in the sample.

Methods

Performance testing included method comparison, detection capability, interference testing, and reference range.

Method comparison
CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Neonatal Patient Samples. Predicate device: ADVIA 1800 Chemistry System.

Detection capability
CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures.

Values were assigned to four individual serum samples using the Atellica CH TBil_2 Assay. These samples were processed on three reagent lots for three days on one instrument for a total of 60 measurements per lot. The mean, SD, %CV, and bias relative to the reference values were calculated for each sample per reagent lot. The lowest sample concentration that met the maximum allowable imprecision and maximum allowable bias acceptance criteria was taken as the LoQ estimate for each reagent lot.

Interference testing
CLSI EP07-A2: Interference Testing in Clinical Chemistry: Approved Guidelines.

Two serum pools at approximately 1.0 mg/dL and 15.0 mg/dL were spiked with HbF, indican, and CYANOKIT.

Reference range
Reference range was conducted according to EP28-A3c for multiple age groups and verified against the reference range found in the following current literature: Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory. Wu AHB, ed. Tietz Clinical Guide to Laboratory Tests. 4th ed. St. Louis, MO: Saunders;2006:172.

Results

Table 1. Regression summary for method comparison.

Specimen Type	Comparison Assay (x)	n	r	Regression Equation	Sample Range
Serum	ADVIA 1800 Chemistry TBIL_2	120	0.983	y = 1.00x + 0.1 mg/dL (2 µmol/L)	0.3–29.8 mg/dL (5–510 µmol/L)

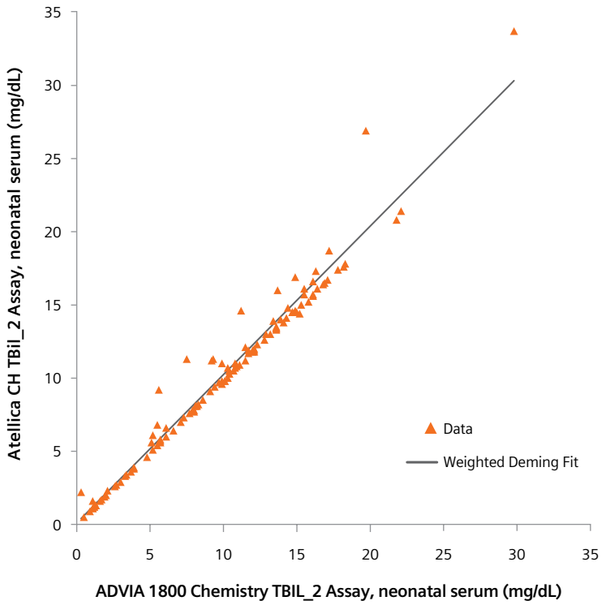

Figure 1. Weighted Deming regression of neonatal serum samples comparing the results from the Atellica CH TBil_2 Assay and the ADVIA 1800 Chemistry TBIL_2 assay.

Detection capability
The LoQ is the lowest amount of total bilirubin that can be determined quantitatively within a defined total error of ≤0.1 mg/dL. The observed LoQ was 0.1 mg/dL (1.71 µmol/L).

Interference testing
Interference testing was conducted for fetal hemoglobin (HbF), indican, and CYANOKIT. TBil_2 was tested at two different analyte concentrations for each interferent. For HbF, interference ranged from -6 to -9%, with higher interference occurring at a lower concentration of total bilirubin. Interference for indican was 0% and ranged from 0 to -2% for CYANOKIT.

Table 2. No significant interference (bias <10%) was observed from 1000 mg/dL HbF, 40 µg/mL CYANOKIT, or 10 mg/mL indican.

Interferent	Interferent Test Concentration	Observed Total Bilirubin Concentration (mg/dL)	Observed Bias
HbF	1000 mg/dL	13.6	-6%
HbF	1000 mg/dL	1.1	-9%
CYANOKIT	40 µg/mL	14.4	-2%
CYANOKIT	40 µg/mL	1.1	0%
Indican	10 mg/mL	14.4	0%
Indican	10 mg/mL	1.1	0%

Reference range

Table 3. More than 20 apparently healthy native serum samples for each reference range were analyzed. More than 95% of the samples from each range were found be within the expected values.

Age Range	Expected Value (mg/dL)	Number of Samples Tested	Samples Within the Reference Range	Samples Outside of Expected Value	% of Samples Outside Expected Value Range
0–1 day	<8.0	30	29	1	3%
1–2 days	<12.0	25	24	1	4%
3–5 days	<16.0	24	23	1	4%
>5 days–60 years	0.3–1.2	24	24	0	0%
60–90 years	0.2–1.1	27	27	0	0%
>90 years	0.2–0.9	21	21	0	0%

Conclusion

The Atellica CH TBil_2 Assay tested on the Atellica CH Analyzer demonstrated acceptable detection capability and interference testing. An existing reference range for neonates and adults was verified with acceptable results. Method comparison results showed acceptable agreement compared to the ADVIA 1800 Chemistry TBIL_2 assay.