Discussion

Accurate and precise bilirubin measurements are critical to the diagnosis and management of hyperbilirubinemia in newborns. As reported in the 2004 American Academy of Pediatrics hyperbilirubinemia guideline, decision levels for repeat bilirubin testing are determined by the age of the infant in hours and the total bilirubin concentration[1]. Other clinical considerations include determining if bilirubin increases are due to hemolytic disorders or congenital abnormalities. The decision to treat infants with phototherapy or exchange transfusion can occur at levels of 15, 20, 25, and 30 mg/dL depending on the infant's gestational age. The College of American Pathologists(CAP) Chemistry Resource Committee recommends that the allowable limits of error for measurements of total bilirubin with commutable reference materials at these decision points should be ± 10%.

To enhance commutability and facilitate bias and accuracy comparisons, specimen NB-01, as for previous educational samples, was manufactured using off-the-clot human serum, and spiked with unconjugated bilirubin to simulate a genuine hyperbilirubinemic neonatal sample. This sample is therefore expected to have minimal matrix effects in comparison to what may be encountered when spiking serum pools with bilirubin surrogate material (ditaurobilirubin) and when using highly processed human or animal serum.

All manufacturers are encouraged to use CAP Surveys data to assess their methods and to investigate differences observed in comparison with other methods. As indicated in the data summary for Sample NB-01, five major instrument manufacturers (Abbott, Beckman, Roche, Siemens, and Ortho) account for more than 92% of all laboratories reporting on the NB/NB2 Surveys. Among the various method/instrument peer groups for these manufacturers, the range of peer group means for bilirubin on sample NB-01 was from a low value of 20.33 mg/dL (347.62 μmol/L) to a high value of 25.81 mg/dL (441.35 μmol/L.) The range of mean biases from the reference method[2] target value was -12.3% to +11.3 %, in contrast with the recommended allowable error limits of ± 10%. However, CAP has been unable to rule out the possibility that mean differences observed for some peer groups with the bilirubin educational sample (sample NB-01 on this cycle) may be attributable to non-commutability (matrix effects.) Therefore, beginning with the present NB/NB2 Survey cycle and going forward, the grading target for the educational samples will be the peer group mean rather than the reference method value; the allowable error limits will remain ± 10%. In cases where a lab's method cannot be assigned to a standard peer group, standard "waterfall" grouping has been applied, ie, Method or All Methods.

The "dual grade" evaluation of specimen NB-01 is provided for educational purposes only and is not reported to Centers for Medicare and Medicaid Services (CMS), nor will it be used by any laboratory accreditation agencies. Specimen NB-01, as with similar educational samples for the NB/NB2 Survey, provides clinical laboratories and manufacturers with information to aid in evaluating the accuracy of their bilirubin method(s). However, performance observed with this sample cannot be considered to be a definitive representation of a method's accuracy.

Each laboratory must assess the accuracy and precision of its instrument/assay system for bilirubin, and if necessary initiate appropriate corrective actions. Participation in (and review of) the NB/NB2 Survey fulfills the evidence of compliance requirement for the CAP Laboratory Accreditation Program Checklist Question CHM.13810.

Neil Greenberg, PhD, DABCC
Chemistry Resource Committee

References

1. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Clinical practice guideline: management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. *Pediatrics.* 2004;114:297-316.
2. Doumas BT, Kwok-Cheung PP, Perry BW, et al. Candidate reference method for determination of total bilirubin in serum: development and validation. *Clin Chem*. 1985;31:1779-1789.