NKDEP Laboratory Working Group Conference Call
November 7, 2006
Conference Call Minutes

Participants
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Tom Hostetter, Albert Einstein College of Medicine
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Summary of Action Items:
- Dr. Marva Moxey-Mims will discuss the possibility of obtaining serum creatinine data along with iohexol measured GFR from the CKiDS Study as well as laboratory analytic method used and creatinine calibration from participating research centers with Dr. George Schwartz.
- Dr. Andrew Narva will communicate the need for obtaining the data from the CKiDS Study prior to the next meeting to Dr. Marva Moxey-Mims and Dr. George Schwartz.
- Dr. John Eckfeldt will look at the commutability study to see if the offset for the major methods at the level of 0.5 mg/dL might provide some guidance in deciding whether a single factor to use in the Schwartz equation is clinically appropriate.
- Nancy Accetta and John Eckfeldt will prepare a list of methods found acceptable by the commutability study for listing on the NKDEP web site and post it when SRM 967 is made available.
- For the list of methods found acceptable by the commutability study, John Eckfeldt will contact each manufacturer to obtain the formal name of the reagent kit and which analyzer was used for each measurement procedure evaluated.
- Dr. Greg Miller will contact the IFCC committee for urinary albumin and albumin/creatinine ratio to explore possible collaboration between NDKEP and IFCC on this topic.

Meeting Minutes

1. **Creatinine Standardization: Report from Whole Blood Subgroup**
   - Dr. John Eckfeldt, Subgroup Chair, reported.
   - Equilibration between the plasma and RBC creatinine can take 5 – 10 hours; therefore, using samples supplemented with creatinine for calibration or performance verification of any whole blood instruments will need to take the equilibration time into account. There appears to be little or no conversion of creatinine into creatine, at least over 24 hours.
   - Two approaches at whole blood calibration seem possible.
     - Collect a set of samples from patients who have mild renal disease and compare results for whole blood with simultaneously collected plasma measure by a reference method (e.g., IDMS, HPLC, or IDMS-traceable clinical method with good accuracy and precision).
     - Use a reference serum (e.g., NIST SRM 967) directly in the whole blood creatinine method to verify accuracy of device's calibration and then use data from an experiment similar to that described above to quantify any whole blood matrix effects. A correction factor may then be applied to convert whole blood results to serum equivalent values.
   - The subcommittee plans to develop bias and precision recommendations similar to those made in the article by Meyers et al. *Clin Chem* 2006;52:5 -18. There is a need for more discussion about how to formulate this. Theoretically, performance characteristics should be the same for whole blood and serum methods, but the actual error is dependent on which reference method is used for equating the whole blood method and the amount of error in that specific method. It is difficult to demand that IDMS be the reference method, so there should be allowance for a lower order reference method traceable to IDMS. However, the effect of using a lower order reference method on the window of acceptability still needs to be defined. The performance characteristics may be difficult to meet for whole blood creatinine methods and the hematocrit correction required for whole blood methods adds to the error. Some methods may not be validated for GFR estimates but could still be used for determining creatinine for dialysis purposes.
   - The group discussed whether there are systematic differences between capillary and venous whole blood creatinine concentrations. ITC is looking at this, and will provide data when they are available.
   - The Subcommittee was unanimous in recommending that whole blood creatinine concentrations be reported as the concentration in simultaneously collect serum.

2. **Creatinine standardization: Report from Non-adult Subgroup**
   - Dr. Harvey Kaufman, Subgroup Chair, reported.
   - Non-adult refers to less than 18 years of age.
   - The group felt that the Schwartz equation is the most commonly used equation for eGFR in non-adults, but there are no data to support this.
   - Small differences in creatinine values within adult reference ranges have a large impact on the eGFR in non-adults, especially premature and term newborn children.
   - The subgroup suggests modifying the Schwartz equation by adding a constant of 0.26 mg/dL to the measured creatinine concentration. There was much discussion about the validation of such an approach. In order to determine valid concentration adjustments, or how to develop a "modified Schwartz equation" to be used with IDMS-traceable creatinine concentrations, measured GFR data for children are really needed. Currently the CKiDS Study is comparing enzymatic creatinine from several clinical sites to HPLC creatinine and measured GFR using iohexol clearance measurements. These data would

be extremely helpful in determining the magnitude of the problem. Dr. Marva Moxey-Mims will discuss with Dr. Schwartz the possibility of obtaining some prepublication access to this information from the ongoing CKiDS study.

- Another suggestion for determining a valid set point was to extrapolate from commutability study at the level of approximately 0.5 mg/dL creatinine; this might provide a method-specific correction factor. Dr. John Eckfeldt will look at the commutability study to see if the offset for the major methods will provide guidance in deciding upon a single factor to use in the Schwartz equation.
- Knowing which equations physicians and pharmacists are using to calculate eGFR in non-adults would be useful. It was suggested that a poll of 10 of the largest children's hospital pharmacies would be enough to determine if most pediatric medical centers are using the same or different equations. Dr. Narva pointed out, however, that the NKDEP cannot collect such information without seeking OMB approval, which is a time-consuming process.

3. Revision of *Suggestions for Labs*

Changes will be reflected on the NKDEP website and the PDF version of *Suggestions*. (LWG members, please see the attached document for changes discussed on the call.)

4. Revision of *Rationale for Use and Reporting Estimated GFR*

Changes will be reflected on the NKDEP website and the PDF version of *Rationale for Use*. (LWG members, please see the attached document for changes discussed on the call.)

5. Next Steps and Action Item Review

- Whole blood subgroup will consider the issue of precision and how to use second order creatinine reference methods in whole blood creatinine method validation.
- Non-adult group will work on providing evidence and legitimacy for using a single constant correction factor in the Schwartz equation.
- Edits will be made to the two NKDEP website documents.
- IFCC has a committee already established to address the issue of accuracy of urinary albumin and albumin/creatinine ratio. Dr. Greg Miller will contact this committee's chair to explore possibilities for cooperation between NDKEP and IFCC. Perhaps there could be a joint meeting of both groups to develop a joint plan and distribute responsibilities.
- There should be a meeting in the first quarter of 2007. Agenda items could include further discussion of the non-adult creatinine measurements and estimating equations, possibly meet with the chair or a subset of the IFCC urinary albumin committee, and additional report from the Whole Blood group. Before the non-adult issues can be discussed, more data from the CKiDS Study would be highly desirable. Dr. Andrew Narva will communicate this need to Drs. Marva Moxley-Mims and George Schwartz.

7. Other Issues

- Status of SRM 967: Dr. Michael Welch reported that the SRM 967 certificate is in review. The date of release is not known at this time, but hopefully will be within a month or so.
- Nancy Accetta will prepare a list of methods found acceptable by the commutability study for the NKDEP web site and post it when SRM 967 is made available. For this list, Dr. John Eckfeldt will contact the manufacturers to obtain the formal name of the reagent kit and which analyzer was used for testing each method.