NKDEP Laboratory Working Group
May 3, 2007 Conference Call Minutes

Participants:

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Summary of Action Items:

- Harvey Kaufman will work with the Estimating and Reporting GFR for Non-Adults Subgroup to develop a precautionary statement regarding the use of eGFR in non-adults; this will be published on the web site and reviewed at the July meeting.
- Information about this precautionary statement needs to be given to John Eckfeldt by June 15 in order to be included in his slides for a Symposium presentation on LWG update at the AACC meeting.
- NKDEP to develop a place on the redesigned web site to serve as a clearinghouse for activities in progress.

Meeting Minutes

1. **Report: International Conference on Standardization in Urine Albumin/Creatinine Measurement and Reporting,** Greg Miller
   The conference was designed to frame issues around albumin and creatinine measurements and determine issues that need to be resolved in order to make recommendations regarding standardization. Some of the issues discussed:
   - Objective of NKDEP is to improve early detection of CKD, facilitate identification of patients at risk and promote evidence based interventions.
   - Adherence to guidelines for at risk populations is poor because albuminuria testing limited in availability, test methods are not standardized, and reporting is not standardized.
   - Cut points by race and gender are needed.
   - Values less than 30 for ACR may be important.
   - Dr. David Bruns reported that the NACB guidelines for diabetes are being updated.
   - EQAS surveys from several countries showed variation of results by method in different countries, poor standardization and a range of imprecision in different methods. In addition, a wide range of sample collection and reporting practices was reported.
   - Dr. Yoshihisa Itoh reported on a Japanese initiative to develop a urine albumin reference material with assigned values based on a diluted serum albumin reference material, CRM470.
   - Dr. John Eckfeldt reported on issues related to collection criteria and concluded that standardization would improve consistency of testing.
   - Dr. Matthew McQueen discussed the variations in the current quantitative albumin methods and that there is uncertainty related to both albumin and creatinine measurements.
   - Dr. Lieske reported on an IDMS reference method that is in development at Mayo Clinic and discussed issues of specificity that are part of their ongoing investigation.

- Dr. Glen Horton described urinary albumin and its role as a measurand; albumin fragmentation may be less in fresh urine than in stored samples making it difficult to interpret results reported in the literature.
- Most manufacturers are using dilution of CRM470 serum reference material for calibration of urinary albumin methods; traceability of calibration of urine creatinine methods is an issue since there is no urine reference material.
- A list of tasks needed to further define the issues was made. Some of the tasks are:
  - Define clinical measurement goals.
  - Define preanalytical requirements.
  - Define specifications for routine method robustness, e.g. determine the pH, osmolality, viscosity ranges, etc. that are expected for urine samples.
  - Define a reference material.
  - Develop a clear definition of the measurand and method specificity requirements.
  - Develop a reference measurement procedure.
  - Publish a report reviewing the current status and issues in urinary albumin testing in a journal such as *Clin Chem*.
  - Develop subcommittees to start working on these tasks.
- The minutes from this conference are under review and will be posted to the web site after they are finalized.
- There is a call scheduled for 5/16 to finalize the minutes and further develop the path forward.
- Status of tasks will be reported at the July LWG meeting.

2. **Report: Whole Blood Measurement of Serum Creatinine,** John Eckfeldt
   A draft of the final report has been sent to committee members for review. The main points are:
   - Creatinine concentration in whole blood samples should be adjusted to be equivalent to simultaneously collected venous serum or plasma values that are traceable to IDMS reference method values.
   - The total error requirements should be the same for whole blood as for venous serum or plasma.
   - Methods for presentation of whole blood measuring accuracy need to be developed that show the uncertainty of the bias and imprecision, specificity requirements need to be clarified, and some acceptability criteria should be developed.
   - The report from this subgroup should be posted on the web site or published in a journal, perhaps as a letter to the editor; a writing group needs to be formed to accomplish this.
   - If an IVD manufacturer lists finger stick or other site capillary whole blood as acceptable, they are obligated to document the comparability to venous whole blood, plasma and serum measurements.

3. **Report: Estimating and Reporting GFR for Non-adults,** Harvey Kaufman
   - The present calculation for eGFR is inconsistent in the non-adult population due to lack of calibration, inconsistency in methods and use of different formulas.
   - The Schwartz equation is being revised for non-adults but is not ready yet.
   - In the interim, recommendations that highlight the shortcomings of the current system and cautioning physicians not to use eGFR in non-adults should be developed for the web site.
   - This subgroup will develop a precautionary statement to be reviewed at the July meeting and for publication on the web site.
   - There is a Symposium at the AACC Annual Meeting on Mon, 7/16, in which John Eckfeldt will present an update on the recommendations; he will need the precautionary statement information from Harvey Kaufman by June 15 in order to include it in his slide presentation.

4. **Report: Status of IFCC Work Group on GFRA,** Neil Greenberg
   - The IFCC has proposed moving to enzymatic methods.
   - A limitation in understanding interferences and developing a specificity recommendation is that most of the available data is over 20 years old so more recent data is needed.
   - One approach is to evaluate specificity using artificial samples but there is a concern about artificial samples because some potential interferents, e.g. ketoacids, would be difficult to simulate because of their volatility. Alternately, samples could be obtained from hospital labs. It is estimated that hundreds of samples would be needed and there are issues of cost and IRB approvals, etc. Assuming a voluntary effort from hospitals and manufacturers for performing the assay, it would cost approximately $50,000 - $100,000 just to obtain the samples.
   - Recommendations need to be based on data from current methods and these would have to be traceable to an IDMS reference method which is very expensive, approximately an additional $50,000 - $100,000.
   - In order to quantify the total error, a range of patient samples would have to be evaluated.

- Funding would be necessary.
- There was a discussion about the applicability of the MDRD equation to other populations, such as the Australian native populations. CKDepi study is looking at several different populations. Andy Levy would be a good contact for this topic because he knows what has been done to date and is collaborating with people from other countries. The problem is that there is not a good gold standard method for actually measuring GFR with which to compare the estimated GFR. IFCC is supporting a group to look at reference ranges in other populations using standardized creatinine methods.

5. Agenda Topics and Planning for the July Meeting in San Diego: 7/17/07 8 am -12 pm

The meeting will be from 8 am – 10:30 am, followed by the manufacturer's forum from 11 am – 12 pm

Agenda topics:

- Urine albumin objectives and activities: Greg Miller plus others from the conference will report.
- Calibration recommendations for whole blood creatinine measurement: John Eckfeldt will present the final report.
- Status of non-adult recommendations: Harvey Kaufman will present the precautionary statement.
  - Update of Schwartz equation: If George Schwartz is attending, he can present this.
  - Guidelines for pediatric drug dosing.
- Creatinine standardization status: Elisa Gladstone will present preliminary data from the survey results; Greg Miller will check if updated CAP survey data will be available by then.
- Review of website redesign: Nancy Accetta will present.
- Recommendations for method specificity: Neil Greenberg will present.
- Manufacturers' Forum: The purpose is to present summary statements to interested people about where we are with various activities of LWG; review of the specificity status; non-adult status; urine ACR status.

6. Redesigning the web site:

Andy Narva suggested creating a place on the NKDEP site's lab section to serve as a clearinghouse for activities in progress.