NKDEP
National Kidney Disease
Education Program

Lab Working Group Meeting
Orlando, FL
July 28, 2005

Members in Attendance
Greg Miller, Virginia Commonwealth University (Chair)
James Fleming, Laboratory Corporation of America
Elisa Gladstone, NIDDK
Neil Greenberg, Ortho Clinical Diagnostics
Glen Hortin, NIH Clinical Center
Gary Myers, CDC
Mauro Panteghini, Università degli Studi di Milano
Frederick Van Lente, Cleveland Clinic Foundation
Harvey Kaufman, Quest Diagnostics
Michael Welch, National Institute of Standards and Technology

Guests
Stephanie Akselrod, Wako Diagnostics
David Armbruster, Abbot Laboratories
Rex Astles, CDC
Christa Cobbaert, EC4 Creatinine Working Group
Mary Lou Gantzer, Dade-Behring
Matt Gnezda, Roche
Chandra Jain, Beckman
Tina Kristensen, Radiometer Medical Aps
Franca Pagani, IFCC
Phil Reavey, Olympus
Bruce Toben, International Technidyne Corporation
Reba Wright, Olympus
Esther Yang, Abbot Laboratories

Status Updates

- Greg Miller introduced a series of status updates on NKDEP and global activities related to the creatinine standardization.
- Greg provided an update on the LN-24 Linearity Survey developed by the College of American Pathologists (CAP) in response to needs of this initiative. (The presentation is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
    - CAP has developed a proficiency testing program using seven specimens. Fresh female off-the-clot serum was used to form the base pool (LN-02); this base pool was spiked with crystalline creatinine to prepare a higher concentration sample (~ 4mg/dL); four

intermediate concentrations were prepared by a gravimetric admixture of the high concentration and base pools; and a low sample (~ 0.5 mg/dL) was prepared by diluting the LN-02 base pool with phosphate buffered saline. The value assignment was done by NIST for the base pool and high pool; concentrations of other pools were calculated by admixture or dilution ratios.

- There have been two mailings: the first in November 2004, the second in May 2005. The first survey had relatively small participation, but there were ~130 participants in the second. Data from this second survey show that a number of platforms have not been recalibrated—per the recommendation of the NKDEP. Roche has already recalibrated their system to be traceable to IDMS; the Dade system appears to have very small bias vs. IDMS (it historically has had the smallest bias of the various peer groups in the field).
- The Participant Summary Report from the May survey was included as a handout, with CAP's permission. The report includes a write-up prepared by Greg and John Eckfeldt advising laboratories how to use this information and reiterates recommendations of the NKDEP Laboratory Working Group.
- For LN-03 and up the coefficients of variation are quite small and very acceptable in terms of intra-laboratory performance, but for lower-concentration samples (LN-02, 0.739 mg/dL; LN-01, 0.501 mg/dL) the imprecision begins to increase rather dramatically. One of the recommendations of the NKDEP therefore is to ask manufacturers to improve performance at the lower concentration levels.
  - Neil Greenberg asked if Greg could share proposed targets in terms of imprecision.
  - Greg shared slides showing total error suggestion for manufacturers: in general, bias should be within 5% of correct and imprecision >8% CV. Data was derived from determining how much change in creatinine (as a result of bias or imprecision) would result in a 10% or less change in estimated GFR value calculated by the MDRD equation.
  - Neil asked if expectation for precision and bias must be the same even at lower levels (e.g., at 0.5 mg/dL). Greg noted that lowest creatinine levels of interest for adults are 0.8 mg/dL or higher; anything lower will yield estimated GFR of >60 mL/min/1.73 m^2, at which point imprecision of measurement creates substantial uncertainty. The NKDEP Laboratory Working Group has not debated an appropriate target specification that would be useful in pediatric environment, the clinical setting in which these lower values become important. A pediatrician has been invited to join the Working Group and help it develop more concrete requirements.
- Greg also shared data from the CAP Comprehensive Chemistry Survey showing that whereas only 3% of labs were reporting estimated GFR in 2003, 20% were reporting it in 2005. But the fact that 80% of labs are still not reporting estimated GFR show there is still far to go.
- Greg closed by noting that the CAP LN24 Survey program is available to anyone who wants to participate, and that hopefully participation will increase so there will be larger peer groups, which will increase confidence in performance measures.

- Mike Welch provided an update on status of new standard reference material. He noted that samples were developed in much the same way as LN-24 samples, as outlined above.

- Mike shared data showing that there is excellent precision with the new LC/IDMS method; very good agreement with certified values from GC/IDMS.
- Used LC/IDMS method for reference material; still need to do GC/IDMS definitive method. Staffing issues have caused a slight delay, but there is a new staff member on board who is starting these measurements in August. NIST hopes to have results in the fall.
- Glen Hortin asked if dilution was best approach for low pool, given protein-related biases. Greg noted that the forthcoming commutability study will identify if there are issues.

- Gary Myers provided update on forthcoming commutability study, the goal of which is to ensure that the high-level reference material (SRM967) is commutable across all the major assays that are currently available. (NOTE: Presentation is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
  - The study will review SRM967, as well as three LN-24 samples: the base pool (LN-02), the high pool (LN-07) and the diluted pool (LN-01).
  - 20 samples (in 0.25 mL aliquots) will be collected from patients in the hypertension, diabetes and transplant evaluation clinics at the University of Minnesota; John Eckfeldt already has received IRB approval for the study.
  - Currently planning to evaluate the following methods, in John Eckfeldt's lab: Beckman CX3, Roche (Jaffé), Roche (enzymatic), Vitros and Dade Dimension. However, the study welcomes any manufacturer who would like to have their assay included or to have the study done in their own application labs. Any manufacturer who would like to be included should contact Gary Myers, Greg Miller or John Eckfeldt.
  - The analytical scheme: routine methods will be run in a single-batch analysis in triplicate, and the reference method (LC/IDMS) will be performed in duplicate measurements.
  - The study should be conducted in August-September 2005; goal is to have the study completed by early fall.
    - Discussion about whether study should take a bit longer so both LC/IDMS and GC/IDMS traceability can be included. Group agreed to talk with John Eckfeldt about this.

- Mauro Panteghini provided an update on IFCC Creatinine Standardization Working Group. (The presentation is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
  - The IFCC now has 75 members, plus 39 corporate and four affiliate members. The Scientific Division, which houses the Creatinine Standardization Working Group, is organized according to theme-oriented committees (n=8) and task-oriented working groups (n=12), including a working group on cystatin C standardization.
  - Mauro also provided an overview of the Joint Committee on Traceability in Laboratory Medicine (JCTLM), which is coordinating ring trials related to serum creatinine. (Only four IDMS labs in the world participating.) Its first task was to publish, in April 2004, a list of approved high-level reference materials and measurement procedures—all of these are GC/IDMS at the moment; no LC/IDMS procedures have been approved yet.

- Current reference materials are not commutable, hence the need for a commutable material such as SRM967. An alternative approach is for manufacturers to split native patient samples and have a reference lab perform a reference measurement procedure to demonstrate comparability, bypassing calibration through use of a secondary material. There is a great need for more reference laboratories, as there are currently only two in the world that are JCTLM approved and able to support manufacturers.
- The IFCC could make a significant contribution by establishing a network of reference laboratories worldwide to provide services with reasonable turnaround time and cost.
- The IFCC established the Creatinine Standardization Working Group to address global issues of coordination and communication. The first meeting was held on July 27, 2005; NKDEP, EC4, the Australian Working Group and JCTLM and the IFCC's Cystatin C Standardization Working Group were represented. The main objectives of the Working Group are to coordinate, support and publicize internationally all activities related to standardizing GFR estimation, and to establish an international reference laboratory network. Neil Greenberg is the proposed chair.
- Goals that emerged from the 7/27 meeting: support international circulation of relevant documents and education materials; preparation of IFCC recommendations regarding the use of enzymatic assays; work with JCTLM to establish an IFCC reference lab network for creatinine; work with NKDEP to develop guidelines to coordinate global introduction of recalibration to be traceable to IDMS together with new GFR estimating equation; and to educate laboratory professionals about the importance of assessing CKD risk.
  - Mike Welch pointed out that the LC/IDMS method is in round two of JCTLM process and he anticipates that it will be approved. Mauro agreed.
  - Neil Greenberg suggested that recommendation regarding use of assays be modified to reflect that goal is to develop more specific assays for creatinine; enzymatic assays are only one approach—there may be alternatives. Mauro agreed.
  - Discussion about the importance of correcting for different ethnicities and identified populations on an international scale, as well as difficulties associated with this (i.e., resistance to identifying race). Fred noted that there will be a handful of defined populations—Pima Indians, Chinese, Danes—to determine if there is international variability. Greg shared e-mail from Andrew Levey (Tufts-New England Medical Center) that there are additional population groups being looked at, but that it will be 9-12 months before the data are available. Greg noted that it would be useful to design studies for other populations, and this is where IFCC could be very helpful.

- Christa Cobbaert provided an update on the activities of the EC4 (European Communities Confederation of Clinical Chemistry and Laboratory Medicine). (The presentation is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
  - As a result of EU-issued IVD directive December 7, 2003 the accuracy of clinical chemistry methods was required to be traceable to highest order reference system available, European labs should be traceable to IDMS methods and thus there is a need to verify the standardization of creatinine measurement using commutable materials.

- An EC4 working group was established that involves six European countries; Joris Delanghe is the chair. First meeting held late 2004 in Amsterdam; participants shared information about the status of creatinine standardization in their countries.
- The working group launched a Trueness Verification Project in 2004 to establish commutability of reference materials across all commonly used field instruments/methods and address intra-laboratory variation. Each of the EC4 members will coordinate with their national EQAS providers to select labs and implement material.
- The project should be implemented in September 2005; data should be available in 2006.

    - Neil Greenberg reinforced the importance of ensuring that all laboratories participating in the study have their instruments properly set up/calibrated so that they yield measurements in conformance to manufacturer's specifications. He proposed emphasizing in communications to labs that they should contact manufacturer representatives to discuss any questions or issues. Christa agreed with this suggestion, and will discuss possible actions with Joris Delanghe. Mauro noted that in Italy, industry representatives were invited to check all the instruments in participating labs before the study begins.

- Rex Astles, on behalf of John Dyke, gave a presentation on a public-private partnership in Michigan to increase use of GFR. (The presentation is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
    - CKD is the ninth leading cause of death in Michigan; the rate of CKD is higher than in other states. So there was agreement to launch a collaboration between the Michigan Department of Community Health and the National Kidney Foundation of Michigan to increase reporting and use of estimated GFR.
    - An expert panel composed of nephrologists, primary care providers, pathologists, laboratory directors, the AACC and CDC was convened in December 2004 to identify and address impediments to implementation of estimated GFR. The panel had three objectives: obtain consensus around the MDRD equation as the current best approach; establish statewide guidelines for the use of estimated GFR as a standard method; and develop practical strategies to encourage clinical labs and to assist in implementation.
    - One key obstacle the panel identified: clinicians are not receptive to receiving reports of estimated GFR because they are not quite sure what to do with it or what its clinical implications are.
    - Baseline data: 22% routinely report GFR, 19% of labs report GFR when ordered and 60% do not report it at all. Of the approximately 40% of labs who provide GFR, about 64% do it onsite, 29% rely on a referral lab, 7% use other hospital personnel.
    - Outcomes of expert panel meeting:
        - Panel members advocated with the Michigan Quality Improvement Consortium, which is currently writing a draft guideline on CKD management and importance of use of estimated GFR; the Michigan Association of Health Plans invited the NKF of Michigan to present finalized guidelines at Fall 2005 meeting of Medicaid Medical Directors.

        - Michigan Association of Health Plans agreed to promote information on GFR in their newsletters; several other health associations have or are planning to disseminate info as well.
        - The state lab will send out letters to all clinical labs advising them of need to provide estimated GFR as part of laboratory reports.

- Published and disseminated Strategic Action Plan for Prevention, Early Detection and Control of Chronic Kidney Disease (available at http://www.nkfm.org/images/KidneyPlanComplete.pdf.)
    - Key lesson learned: value of using both traditional and non-traditional public and private partners; importance of state taking the lead to develop and disseminate guidelines.
    - Rex also mentioned that he has heard that there is a bill in the US Senate to provide funds that the CDC could pass along to states promote CKD surveillance and use of eGFR, and there is a bill in the Michigan Senate proposing that managed-care organizations that receive Medicaid reimbursement must contract with labs that report calculated GFR.
    - Rex also noted that CDC has a strong relationship with the 50 state laboratories, and that the Michigan program provides a good model for how state labs can work effectively with private clinical labs.
        - Neil Greenberg asked if there is an opportunity to measure the success of the program, especially in terms of patient outcomes. Rex answered that at least we can measure process changes in laboratories re estimated GFR reporting.
        - Glen Hortin noted importance of involving pharmacists in programs such as this; Rex agreed.
        - David Armbruster noted that having data on patient outcomes as a result of increased use of GFR would help clinical chemists educate clinicians about its value.
        - Harvey Kaufman asked if physician resistance to GFR might be overstated, citing a Pittsburgh-area pilot in which Quest offered an opt-out approach to receiving estimated GFR, and only one doctor opted out. Rex offered opinion that perhaps no one wanted to opt-out, even if they were not going to use the data, due to liability concerns.
        - Greg noted that NKDEP has received funding for evaluation studies of increasing lab reporting of estimated GFR.

- Fred Van Lente provided an update on the status of the revised estimating equation, speaking informally due to the fact that abstract on revised equation was still under review.
    - Measured material on both the Beckman CX3 Delta and Roche enzymatic. The Roche method hit the IDMS targets exactly. The CKD-EPI team then used calibration adjustment to correct the CX3 Delta method results to the Roche enzymatic method. There was an approximately 0.95 relationship between CX3 and Roche methods.
    - The revised MDRD equation will be officially presented at the American Society of Nephrology meeting in November.
    - The CKD-EPI project is also looking at cystatin C, and developing a cystatin C estimating equation. Although data is forthcoming, Fred predicted that it is unlikely cystatin C will displace serum creatinine in estimating GFR.

- Greg reinforced that the revised MDRD equation should only be used with serum creatinine levels that have been derived from IDMS-traceable methods.
- Fred said that there might be some confusion related to the fact that Roche enzymatic works fine, but that other methods will need to be recalibrated to be IDMS traceable.

- Discussion about whether the NKDEP should recommend an interim correction factor (adding a small bias to serum creatinine measure) for methods that are currently IDMS traceable prior to availability of revised equation. There was concern that given lag time in disseminating information through laboratory community, an interim correction might only add confusion. It was agreed that the NKDEP would not recommend an interim correction factor and simply wait until revised MDRD is available.
- Gary Myers provided an update on the *Clinical Chemistry* manuscript. He received and responded to two sets of editorial comments, and is awaiting further comments from one more reviewer. Should have an update on the status of the manuscript shortly. Gary walked through the recommendations in the manuscript, noting that they have been organized by audience.
  - <u>Key recommendations for IVD manufacturers</u>:
    - IVD manufacturers and clinical labs should coordinate introduction of re-calibration to IDMS to coincide with a revised GFR estimating equation based on creatinine values traceable to IDMS
    - NKDEP will have a revised equation in 2005
    - Clinical laboratories should report estimated GFR as >60 mL/min/1.73 m^2 when values are above 60
    - Report serum creatinine values as mg/dL to two decimal places. Values reported as µmol/L should be reported as the nearest whole number.
    - IVD manufacturers should target optimal creatinine method performance at 1.0 mg/dL (88 µmol/L), and ensure comparable trueness and precision throughout the AMR
    - Precision at lower creatinine concentrations needs to be improved to allow acceptable estimated GFR at values >60 mL/min/1.73 m^2, and for pediatric populations
    - After re-calibration to IDMS, a realistic total error goal for creatinine is a maximum 10% increase in the relative error of the estimated GFR
      - Typical values: bias <5%, and CV <8%, at creatinine 1.0 mg/dL (88 µmol/L)
    - IVD manufacturers must address analytical non-specificity in current routine methods

  - <u>Key recommendations for NKDEP in collaboration with other professional organizations</u>:
    - Identify the impact on clinical decision criteria that may result from re-calibration of serum creatinine to be traceable to IDMS
    - Develop a replacement for the MDRD equation that uses serum creatinine measurement traceable to IDMS
    - Coordinate introduction of method traceability to IDMS with the appropriate GFR estimating equation

- Develop guidelines to implement appropriate GFR estimating equations for re-calibrated creatinine and to communicate the resultant changes in clinical interpretation of serum creatinine
- Communicate the clinical issues associated with re-calibrated serum creatinine
  - Reference interval change
  - Creatinine clearance values and reference interval change
  - Pharmacy impact on drug dose adjustment
  - Pediatric GFR estimating equations
- Coordinate with PT/EQAS providers to ensure appropriate grading adjustments are made during transition to IDMS traceability
- Establish a small group of reference labs that can perform high throughput reference measurement procedures
- Implement educational programs on the proper use of the MDRD equation to assess CKD risk.

o <u>Key recommendations for National Metrology Institutes, reference laboratories, and members of JCTLM:</u>

- Provide tools to assist IVD manufacturers to reduce analytical bias, since many routine methods can meet or exceed the imprecision goal of <8%
  - By the end of 2005, develop commutable reference materials for serum creatinine (NIST SRM967 is expected to fulfill this need when available)
  - By the end of 2005, make available LC-IDMS reference method. Additional reference laboratories will be needed to meet the anticipated demand

o <u>Key recommendations for PT and EQAS providers:</u>

- Introduce a regularly recurring proficiency program that uses commutable serum materials with target values traceable to IDMS reference measurement procedures
  - Permits an ongoing assessment of routine method performance and the evaluation of accuracy transfer processes used by manufacturers
  - The CAP Creatinine Accuracy Calibration Verification/Linearity Survey (LN-24) has these attributes

o Gary confirmed group decision to delete from the manuscript the interim recommendation that a correction factor be added to serum creatinine value for re-calibrated methods

o Mauro asked about a statement that many methods could meet/exceed imprecision targets. Gary acknowledged that not all methods will be able to meet them, especially at low values.

o Neil proposed that EQAS providers be alerted that there will be a transition period in which they may see two different populations (some will have re-calibrated, others will not) so labs are not unfairly penalized. It was suggested that establishing different peer groups might be the answer, and that manufacturers should communicate their plans and schedule to EQAS providers. The NKDEP Laboratory Working Group will also inform EQAS

providers about our general plans and timeline—and when they should expect to hear from manufacturers about their specific plans.

Proposed Project Timeline for Recalibration of Creatinine Methods

- Revised estimating equation will be available in November 2005; further validation for other ethnic groups, with possible further revisions to equation, may occur 2006-2007.
- SRM967, with commutability validation, will be available in late 2005 or early 2006.
  - The group discussed getting fast-track JCTLM approval the for LC/IDMS method for SRM967, and whether rollout of recalibration efforts will be contingent upon the proposed reference materials (i.e., SRM967) being accepted by JCTLM.
    - Neil suggested that it is possible for manufacturers to implement recalibration prior to acceptance by JCTLM; there seemed to be general consensus around this.
    - Gary noted that a possible alternative might be for manufacturers to use reference labs instead, though there may be an issue because there are only two labs worldwide that currently provide measurement services (it may take three months or longer).
    - JCTLM approval of SRM967 could happen by early 2006.
  - The transition to new calibration of routine methods is expected to take 6-24 months—should be complete in late 2007 or 2008.

Pharmacy Objectives

- Leigh Ann Milburn (PharmD, BCPS), a clinical pharmacy specialist at St. Luke's Hospital, has accepted NKDEP's invitation to serve as pharmacy liaison to the Laboratory Working Group
- She was unable to attend the meeting, so shared some of her perspectives via a memo, which is available on the NKDEP website at http://www.nkdep.nih.gov/about/workinggroups/laboratory.htm#meeting.)
- Harvey noted that we should also consider engaging anesthesiologists to learn if there are drugs used in operating room that pharmacists might not be familiar with.
- Neil reinforced that the standardization process has major implications for pharmacists, and asked if the NIH could make funds available to the pharmacy community so they could conduct and publish studies using the revised MDRD equation. Elisa Gladstone agreed to explore the feasibility of this.
- Mauro reinforced the pharmacy liaison's comment that recalibration efforts also would have a profound impact on reference values for creatinine clearance, which are used in current dosing guidelines and computerized dosing applications.

Reference Range Recommendations

- Greg led a discussion of whether NKDEP should recommend to laboratories not to provide a reference range for serum creatinine, and to rely solely on estimated GFR. He outlined three possible scenarios:
  - Manufacturers could provide magnitude of calibration change as a correction factor to the creatinine reference range

- Replace traditional reference ranges with estimated GFR as a standardized clinical interpretation of creatinine
- Creatinine clearance reference range will be clinically different and should be discontinued.

- Manufacturers shared concerns about the implications the recommendation to no longer provide reference range information would have for their labeling, and whether they would need to submit revised labeling to the FDA. It was noted that introduction of estimated GFR could be viewed by the FDA as a new claim, which would require a lengthy review process. (Greg noted that Ethan Hausmann from FDA is a member of the Laboratory Working Group and could be consulted on this.)
  - Fred Van Lente noted that there may be a problem replacing reference range intervals with GFR given accuracy of the estimating equation across all audiences and levels of kidney function (e.g., values greater than 60 mL/min/1.73 m^2)
  - Harvey reinforced Fred's point that clinicians will want to know more what serum creatinine is when estimated GFR is greater than >60 mL/min/1.73 m^2; others agreed and noted that same may hold true with pediatric patients.
  - Neil suggested that instead of recommendation to "replace" reference ranges with estimated GFR, the NKDEP should propose to "augment" or "supplement" because creatinine is still very useful in certain instances.
- Greg explained that rationale behind the recommendation was that studies show physicians often misinterpret serum creatinine against conventional reference ranges and fail to recognize patients that should be referred or followed up with for CKD. In conclusion it was agreed that the conventional reference range for creatinine should be retained.
- Greg then asked the working group to consider creatinine clearance: should we recommend that creatinine clearance be phased out or limited in scope and replaced by estimated GFR? He noted that the data show that estimated GFR is a more reliable indicator of kidney function than measured creatinine clearance.
  - Fred noted that that the K/DOQI guidelines have already made this recommendation
  - It was agreed that NKDEP would make this recommendation only for adults, but include a statement regarding use in pediatric patients cautioning clinicians that recalibration will result in inaccurately high values for creatinine clearance and that they should take this into consideration when interpreting results.

Communications Plan

- Greg presented a draft communication plan developed by NKDEP to inform various audiences (e.g., IVD manufacturers, laboratories, providers) about the creatinine standardization process as well as the NKDEP recommendations for each audience. The plan includes messages and proposed tactics.
  - The plan includes a proposal to invite people to register for a listserv on the NKDEP website, as well as a form for submitting questions. It was agreed that questions will be managed by the NKDEP staff, which will also create a FAQ page once it becomes clear what these are.

- The group suggested that in addition to asking relevant third-party organizations to include links to the NKDEP website (as proposed in the plan), we should also seek to have them post information directly on their website to make it more easily accessible.
- The group agreed to use the publication of the paper in *Clinical Chemistry* as a hook for outreach to relevant trade media.
- The group suggested that NKDEP recommendations be included in all LN-24 mailings over the next two years (four mailings in all).

- Neil suggested that creatinine standardization information/recommendations be presented not just as coming from NKDEP, but as being jointly developed by NKDEP, IFCC, AACC, EC4 and other groups. Greg agreed that there has been broad, global participation in this project and that it would make sense to explore more formal relationships with other groups as well as opportunities for co-branding materials.
  - It was agreed that while it is important to have close coordination of messages, materials and activities among all groups who will be communicating about standardization, it will be important to avoid lengthy review processes by partners so as not to sacrifice timeliness. As such, it was agreed that we would rely upon general consensus rather than establish a process for formal review and endorsement—although Greg pledged that representatives to the Laboratory Working Group would have an opportunity to review materials before they were posted on the NKDEP website.
- It was suggested that AACC's Laboratory Tests Online might be a useful communications partner, along with several other medical information websites. Greg suggested that these opportunities could be explored through the NKDEP's Professional Working Group.
- Greg confirmed that everyone in attendance supported updating the NKDEP website with the recommendations from the draft manuscript (see pp. 7-8 above), with the understanding that the interim recommendation regarding adding a correcting bias will be deleted. The NKDEP will postpone decisions/actions on other issues until there is broad agreement on them.
- Greg then reviewed the Suggestions for Laboratories document and captured comments from the group—including deleting the interim recommendations, revising the description about the MDRD equation (from "is widely accepted" to "has been shown to be the best…"), including SI unit equivalencies, removing table of serum creatinine reference ranges, and minor edits.
  - Greg agreed to revise the document per the group's suggestions.
- NKDEP will update the website with revised Suggestions for Laboratories and downloadable information sheets outlining NKDEP recommendations for each key audience.

Closing

- Greg outlined key next steps:
  - Deploy the standardization program—with a two-year timeframe in which to complete implementation of traceability and new estimating equation. The group's recommendation is to have manufacturers begin this process in 2006, coordinating recalibration to IDMS-traceable reference materials along with adoption of the new estimating equation.

- Deploy the communication/education program as outlined in the plan. Greg noted that it might make sense to ask several members of the NKDEP Laboratory Working Group to serve on a subgroup who could advise on this project.
- Coordinate with IFCC and other professional organizations.
- Coordinate with pharmacy community and their professional organizations.
- Inform LIS/HIS computer software providers about the standardization program. NKDEP will reach out to appropriate industry trade groups for LIS manufacturers, and inquire about presentation or poster at one of their conferences.
    - Mary Lou suggested we ask Jerry Goldsmith at AACC about LIS contacts; Greg noted that we should also engage AACC informatics division.
- Develop guidelines for pediatric estimating equations. Greg noted that the NKDEP has invited a pediatric representative to participate in the Laboratory Working Group to advise on issues in the pediatric population.
    - Christa asked whether standardization will have an impact on the Schwartz equation used in pediatric settings.
    - Greg proposed adding language to laboratory reports for patients under 18 about the impact of standardization on creatinine measurements, as well as putting language on website around the same time that the new equation is available, advising caution in use of pediatric estimating equations because recalibrated creatinine will give lower values which will produce higher estimated GFR values with all current equations.
    - Mauro suggested cystatin C may provide another alternative approach for pediatrics.

- The next Laboratory Working Group meeting will be held most likely early in 2006 to continue discussion. It was agreed that a conference call and/or web meeting might be the most efficient approach for this next meeting.