



MEMORANDUM # 78

**TO:** UNC Hospitals Attending Physicians, Housestaff, Department Heads, Nursing staff and Supervisors

**FROM:** John F. Chapman, Dr. P.H., Professor and Director, Core Laboratory *JF*

*RJF* Ronald J. Falk, M.D., Professor and Chair, Division of Nephrology and Hypertension

*MST* Melanie S. Joy, Pharm.D., Associate Professor, Division of Nephrology and Hypertension

*CB* Connie Bishop, Assistant Administrative Director, Core Laboratory

*MB* Mark Brecher, M.D., Professor and Chair, McLendon Clinical Laboratories

*CH* Cathy Holleman, Admin. Director, McLendon Clinical Laboratories

**SUBJECT:** Change to IDMS calibration for Serum and Urine Creatinine

**DATE:** May 13, 2008

Effective May 23, 2008 at 12:00 midnight, in accordance with the recommendations of the National Kidney Disease Education Program (NKDEP), the calibration of all serum and urine creatinine results will be modified to enable traceability to the internationally accepted isotope dilution mass spectrometry (IDMS) reference method.<sup>1</sup> This change to standardized creatinine values is expected to improve detection, diagnosis and treatment of chronic kidney disease by reducing inter-laboratory bias and yielding more uniform estimates of GFR when using the MDRD equation for estimating eGFR.

The absolute change in serum creatinine values from our current calibration method will be modest, with the greatest impact on lower values. However, this will have a significant impact on eGFR and creatinine clearance calculations. Other than the use of IDMS-traceable standardization, our enzymatic creatinine serum and urine methods introduced in 1997 will remain unchanged. Details of the changes in post-IDMS reference range values and conversion factors are shown on page 3.

Impact on MDRD eGFR Calculations:

After this change, eGFR estimates will continue to be automatically calculated and reported in the Clinical Information System (CIS) for all subjects 18 years or older using the updated (MDRD) equation. Although this change should improve accuracy of the estimate at higher estimated GFR levels, in accordance with current NKF recommendations, calculated values above 60 mL/min/1.73m<sup>2</sup> will continue to be reported as "≥60 mL/min/1.73m<sup>2</sup>". Calculated GFR values <60 mL/min/1.72m<sup>2</sup> will continue to be reported as the actual calculated number with an accompanying "L" flag. Those of you wishing to calculate eGFR manually must be sure to use the updated equation: (estimated GFR (mL/min/1.73m<sup>2</sup>) = 175 x (Sc<sub>r</sub>)<sup>-1.154</sup> x (Age)<sup>-0.203</sup> x (0.742 if female) x (1.210 if African-American)).

Post-IDMS serum creatinine values will be somewhat lower than previously reported values. This will produce **increases** in reported eGFR values ranging from 4-10% as compared with pre-IDMS creatinine-based estimates.

Although the MDRD equation has been shown to be a more accurate GFR estimate than creatinine clearance measurements from 24-hour urine collections<sup>2</sup>, there are exceptions where the latter may be required:

- Extremes of age (<18 and >70) and body size
- Severe malnutrition or obesity
- Disease of skeletal muscle
- Paraplegia or quadriplegia
- Vegetarian diet
- Rapidly changing kidney function
- Prior to dosing drugs with significant toxicity that are excreted by the kidneys
- Pregnancy

Impact on Creatinine Clearance Calculations using 24 hr urine collections:

As indicated above, post-IDMS serum creatinine values will be somewhat **lower** than previous whereas urine creatinine values >15 mg/dL will be only marginally affected. This would be expected to produce **increases** in calculated creatinine clearance averaging 14-18% compared with pre-IDMS creatinine-based calculations. Our in-house studies on healthy subjects show the following relationship between 24 hr creatinine clearance calculations pre- and post-IDMS calibration:

FEMALES: IDMS Creatinine clearance = 1.14 \* Previous creatinine clearance + 0.04.

MALES: IDMS Creatinine clearance = 1.18 \* Previous creatinine clearance – 2.50.

Questions? Call Core Lab Customer Service @ 6-2361.

References:

<sup>1</sup> Myers, GL, Miller GW, Coresh J, et al. Recommendations for improving serum creatinine measurement: a report from the Laboratory Working Group of the National Kidney Disease Education Program. *Clin Chem.* 2006;52:5-18.

<sup>2</sup> Levy AS, Bosch JP, Breyer Lewis J et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation.. *Ann. Int. Med.* 1999;130:461-470.

## REFERENCE RANGE AND CONVERSION TABLES

<b>Serum/Plasma</b>								
Current Reference Range				Post-IDMS Reference Range				
Age/Sex	LL mg/dL	UL mg/dL	µmol/L (SI Units)	Age/Sex	LL mg/dL	UL mg/dL	LL µmol/L (SI Units)	UL µmol/L (SI Units)
0-7d	0.6	1.1	53.0-97.2	0-7d	0.5	1.0	44.2	88.4
8d-1mo.	0.3	0.7	26.5-61.9	8d-1mo.	0.2	0.6	17.7	53.0
1mo-2yr	0.3	0.6	26.5-53.0	1mo-2yr	0.2	0.5	17.7	44.2
3-4yr	0.3	0.7	26.5-61.9	3-4yr	0.2	0.6	17.7	53.0
5-9yr	0.4	0.9	35.4-79.6	5-9yr	0.3	0.8	26.5	70.7
10-17yr/Male	0.5	1.1	44.2-97.2	10-17yr/Male	0.4	1.0	35.4	88.4
10-17yr/Female	0.4	1.0	35.4-88.4	10-17yr/Female	0.3	0.9	26.5	79.6
18yr+/Male	0.8	1.4	70.7-123.8	18yr+/Male	0.7	1.3	61.9	115.0
18yr+/Female	0.7	1.1	61.9-97.2	18yr+/Female	0.6	1.0	53.0	88.4
<b>CONVERSION FACTORS</b>								
Post-IDMS serum creatinine (mg/dL) = old serum creatinine (mg/dL) * 0.93 – 0.062								
Old (non-IDMS) serum creatinine (mg/dL) = Post-IDMS serum creatinine (mg/dL) ÷ 0.93 + 0.062								

<b>24 hr Urine: Values &gt; 14mg/dL:</b>				
Current Reference Range				Post-IDMS Reference Range <b>NO CHANGE</b>
	LL mg/24h	UL mg/24h	(SI Units) µmol/24h	
ADULT	800	2800	7,070- 24,750	
<b>CONVERSION FACTORS</b>				
Post-IDMS Urine Creatinine (mg/dL) = old urine creatinine (mg/dL)*1.01 – 2.4				
Old (non-IDMS) Urine Creatinine (mg/dL) = post-IDMS urine creatinine (mg/dL) ÷ 1.01 + 2.4				
<b>Urine Values ≤14 mg/dL:</b>				
Use same conversion factor as serum/plasma above				