

## Creatinine Assay Restandardization and Revised Reference Ranges

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The creatinine assay performed in the Danbury Hospital Laboratory has been restandardized. Creatinine results reported by our laboratory will now be traceable to the internationally accepted isotope-dilution mass spectrometry (IDMS) reference method. This restandardization is part of a global effort that is being spearheaded by the National Kidney Disease Education Program (NKDEP), whose goal is to reduce interlaboratory variation in serum creatinine measurements and therefore improve the accuracy of glomerular filtration rate estimates (eGFR).

### Effect on creatinine results and reference (normal) values

Creatinine values obtained with the new IDMS-standardized assay will be lower than values with the old non-IDMS assay. The average difference observed at various serum creatinine concentrations and the changes in reference ranges are:

Old Non-IDMS Creatinine (mg/dL)	New IDMS Creatinine (mg/dL)	Expected Difference (mg/dL)
0.50	0.41	-0.09
1.00	0.88	-0.12
2.50	2.29	-0.21

Serum Creatinine Reference Ranges (mg/dL)		
	Old Range	New Range
Male	0.80-1.50	<b>0.69-1.31</b>
Female	0.70-1.20	<b>0.60-1.04</b>

The new reference ranges have been verified with local population studies using serum from healthy volunteers in the Danbury area. Laboratory reports will include a comment alerting physicians to the new ranges for one month.

### Effect on eGFR calculated with the MDRD equation

We will continue to calculate values for estimated glomerular filtration rate (eGFR) and report these values with patients' serum creatinine results as recommended by NKDEP to assist physicians in identifying and monitoring patients with chronic kidney disease. The lower serum creatinine results obtained with the restandardized

#### **KEY POINTS:**

- **Our creatinine assay is being restandardized.**
- **Serum creatinine values will be lower by  $\cong 0.1$  at 1.0 mg/dL and  $\cong 0.2$  at 2.5 mg/dL.**
- **New reference ranges for serum creatinine: Male: 0.69-1.31 mg/dL, Female: 0.60-1.04 mg/dL**
- **Estimated GFR values included in lab reports will not be affected.**
- **Cockcroft-Gault GFR estimates will be slightly higher; the Pharmacy will consider this when recommending dose adjustments in patients with renal impairment.**

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creatinine assay will not affect these eGFR values because the MDRD (Modification of Diet in Renal Dialysis) equation used for the eGFR calculation has also been adjusted to reflect the new creatinine standardization.

The new MDRD equation is:

$$\text{eGFR} = 175 \times (\text{S}_{\text{cr}})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$$

An on-line GFR calculator based on the new MDRD equation can be found on the NKDEP website at: [http://www.nkdep.nih.gov/professionals/gfr\\_calculators/idms\\_con.htm](http://www.nkdep.nih.gov/professionals/gfr_calculators/idms_con.htm).

### **Effect on eGFR calculated by the Cockcroft–Gault equation and drug dose calculations**

Drug dosing is generally based on pharmacokinetic studies where kidney function is assessed using estimates of creatinine clearance/GFR obtained by the Cockcroft-Gault (C-G) equation. For the majority of patients, the difference in GFR estimates from the MDRD and C-G equations will not lead to a difference in drug dosages; however, if the estimates differ, the literature recommends that the C-G value be used in order to be consistent with pharmacokinetic studies. Please be aware that unlike the MDRD equation, the C-G equation has not been adjusted to account for the shift in IDMS-traceable serum creatinine compared to conventional (non-IDMS traceable) creatinine. Therefore, the lower serum creatinine values obtained with IDMS-traceable assays will give somewhat higher GFR estimates with the C-G equation that in some instances may result in calculated doses for a given drug that are higher than doses calculated using conventional (non-IDMS) creatinine values. The Danbury Hospital Pharmacy is aware of the effect of lower serum creatinine values on C-G calculations and will consider this when recommending drug dose adjustments for patients with impaired renal function.

**Effective Date:** The new creatinine assay will be implemented on November 3, 2008.

### **References**

1. For details about the Creatinine Standardization Program, see: [http://www.nkdep.nih.gov/labprofessionals/creatinine\\_standardization.htm](http://www.nkdep.nih.gov/labprofessionals/creatinine_standardization.htm)
2. For on-line GFR calculator, see: [http://www.nkdep.nih.gov/professionals/gfr\\_calculators/idms\\_con.htm](http://www.nkdep.nih.gov/professionals/gfr_calculators/idms_con.htm)