

# New Methods for Measuring Serum Creatinine

Implications for pharmacists and authorized drug prescribers

from a release issued by the National Kidney Disease Education Program

**T**he National Kidney Disease Education Program (NKDEP), in collaboration with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Communities Confederation of Clinical Chemistry (EC4), has launched the Creatinine Standardization Program to reduce inter-laboratory variation in creatinine assay calibration and provide more accurate estimates of glomerular filtration rate (GFR). The effort is part of a larger NKDEP initiative to help health care providers better identify and treat chronic kidney disease in order to prevent or delay kidney failure and improve patient outcomes.

The NKDEP has recommended that all laboratories report estimated GFR (eGFR) along with serum creatinine measurements to assist physicians and other health care providers with recognition of early kidney disease. Most currently available clinical methods for serum creatinine have a small, but somewhat variable, positive bias due to interfering substances in normal serum.

As a result, better inter-laboratory standardization of serum creatinine is necessary to support standardization of eGFR and its use in clinical guidelines for kidney disease.

Clinical laboratory methods for serum or plasma creatinine are being re-calibrated to produce values that agree with an isotope dilution mass spectrometry (IDMS) reference method. The recommended equation to estimate GFR was developed from the Modification of Diet in Renal Disease (MDRD) Study using a creatinine method with a slight positive bias. A new version of this equation is now available that has correct coefficients for serum cre-

atinine methods that have been calibrated to agree with IDMS.

Clinical guidelines used by pharmacists to adjust drug dosages for patients with impaired kidney function are usually based on estimating equations for creatinine clearance (e.g., Cockcroft-Gault). These estimating equations were developed using serum creatinine methods that had a positive bias to the IDMS reference method of about 10-20%. When laboratories recalibrate serum creatinine methods to remove that positive bias, a patient's creatinine result will become lower, in most cases. In addition, estimates of kidney function using any of the estimating equations or algorithms derived from older creatinine methods will become higher by roughly the same percentage. Depending on the analytical system used by the clinical laboratory, and how that method calibrates urine creatinine measurements, the creatinine clearance calculated from serum and urine measurements either will be unaffected by the recalibration of creatinine or may increase slightly.

Pharmacists and drug prescribers should contact their clinical laboratory to determine if a creatinine method with calibration traceable to IDMS has been put in service. In turn, the clinical laboratory should notify pharmacists and drug prescribers of the expected magnitude of change in serum creatinine values, and whether the creatinine clearance measured from serum and urine will be affected by the change.

The following points should be considered:

- Following implementation of revised calibration for serum creatinine methods, use of the IDMS-traceable MDRD Study equation will give an accurate value for eGFR in adults.
- The serum creatinine reference interval will change, in most cases, to lower values. The magnitude of change is likely to be between 5-20%.

- Creatinine clearance values based on measured serum and urine creatinine results may change. A new reference interval and interpretive criteria may need to be established for creatinine clearance. The effect on measured creatinine clearance will vary depending on the procedures used to calibrate serum and urine measurements.

- Following implementation of revised calibration for serum creatinine methods, creatinine clearance estimating equations such as Cockcroft-Gault, Schwartz, or Counahan-Barratt will, in most cases, give values that are higher than the values obtained before creatinine method recalibration. Individual institutions will need to determine the clinical implications of these higher values. In many instances, the change may have little clinical significance for drug dose decisions. Institutions may wish to refer this issue to a multidisciplinary team (e.g., clinical decision support team) to determine the impact of creatinine calibration changes at their institution.

- For identifying and staging chronic kidney disease (CKD), an eGFR using the MDRD Study equation is more accurate than creatinine clearance calculated from serum and urine measurements for most patients. Therefore, NKDEP recommends not performing a measured creatinine clearance procedure for adults except when the patient's basal creatinine production is very abnormal. This may be the case with patients of extreme body size or muscle mass (e.g., obese, severely malnourished, amputee, paraplegics or other muscle-wasting diseases) or with unusual dietary intake (e.g., vegetarian, creatine supplements).

- For drug dosing purposes, NKDEP does not recommend using the MDRD Study equation at this time because the clinical impact on drug dose adjustment has not been compared between current practice and the MDRD Study equation. Pharmacists should continue to use their




SUGGESTIONS FOR LABORATORIES  
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 LABORATORY\\_REPORTING.HTM](http://WWW.NKDEP.NIH.GOV/RESOURCES/LABORATORY_REPORTING.HTM)

current drug dosing methods.

• Pharmacists should keep in mind that the MDRD Study equation is an important tool for identifying patients at risk for CKD. These patients are at high risk for developing drug-related problems. Utilizing the MDRD Study equation to identify patients at risk for CKD provides pharmacists an opportunity to collaborate with physicians in optimizing medical management of these patients.

The Laboratory Working Group of NKDEP is collaborating with the American Society of Health-System Pharmacists to discuss the impact of the above issues on pharmacists and patient care. ●

 MORE INFORMATION ABOUT THE CREATININE STANDARDIZATION PROGRAM AND RECOMMENDATIONS FOR OTHER GROUPS, INCLUDING CLINICAL LABORATORIES, ARE AVAILABLE AT [WWW.NKDEP.NIH.GOV/LABPROFESSIONALS](http://WWW.NKDEP.NIH.GOV/LABPROFESSIONALS)

These recommendations update those originally published in *Clinical Chemistry* 2006;52(1):5-18. For assistance, please contact the NKDEP at [esp@info.niddk.nih.gov](mailto:esp@info.niddk.nih.gov) or call 301-435-8116.



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FDA is launching a new program to make drug safety information available to you in an easily accessible format. Because patients are taking a more active role in their health care, we want to make safety information available about the medicines they are using. We believe that patients, their health care professionals, and other consumers will find the information we are providing useful in their prescribing and treatment decisions.

Our Drug Safety Initiative has the following components:

- **Index to Drug-Specific Information.** For patients, consumers, and health care professionals. Provides links to safety sheets with the latest risk information about the drug, related press announcements, and other fact sheets.
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- **Draft Guidance: FDA's "Drug Watch" for Emerging Drug Safety Information**
- **Federal Register Notice of Availability -- Draft Guidance for Industry on the Food and Drug Administration's "Drug Watch" for Emerging Drug Safety Information (5/10/2005)**
- **Manual of Policies and Procedures (MaPP): Drug Safety Oversight Board (DSB)**
- **Drug Safety Oversight Board Members**
- **Drug Safety Oversight Board Meetings: Public Summaries**
- **Questions and Answers on FDA's New Drug Safety Initiative**
- **"Keeping Up With Drug Safety Information,"** May, 2006 article from FDA Consumer magazine
- **Secretary Leavitt's February 2005 press release**

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