

# **Creatinine Measurement**

**NKDEP Manufacturers' Forum**

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# Creatinine bias vs. RMP over time

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**RMP value = 0.86 mg/dL      0.90 mg/dL**  
**Bias 1994<sup>a</sup>                      Bias 2003<sup>b</sup>**

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<b>Beckman CX</b>	<b>0.08</b>	<b>0.12</b>
<b>Dade Dimension</b>	<b>0.08</b>	<b>0.06</b>
<b>Roche 717/747</b>	<b>0.22</b>	<b>0.00</b>
<b>Olympus</b>	<b>0.13</b>	<b>0.11</b>
<b>Ortho Vitros</b>	<b>0.14</b>	<b>0.10</b>

<sup>a</sup> Arch Pathol Lab Med 1998;122:587-608

<sup>b</sup> Arch Pathol Lab Med 2005; 129:297-304

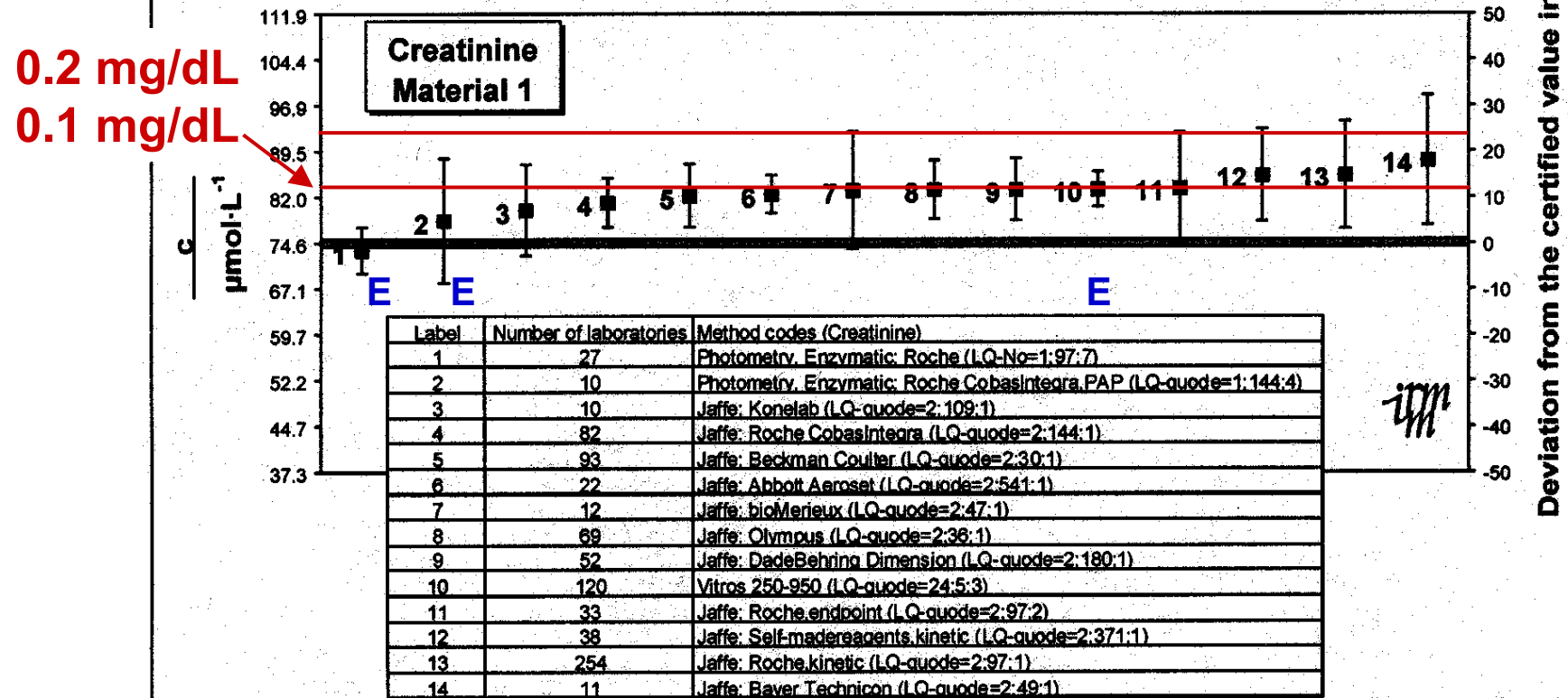
# IMEP-17, 2002, Fresh Frozen Serum, N = 833

## Creatinine = 0.84 mg/dL (74.6 μmol/L)

VERTICAL BARS = ±1 SD for distribution of participant results

IMEP- 17: Trace and minor constituents in human serum

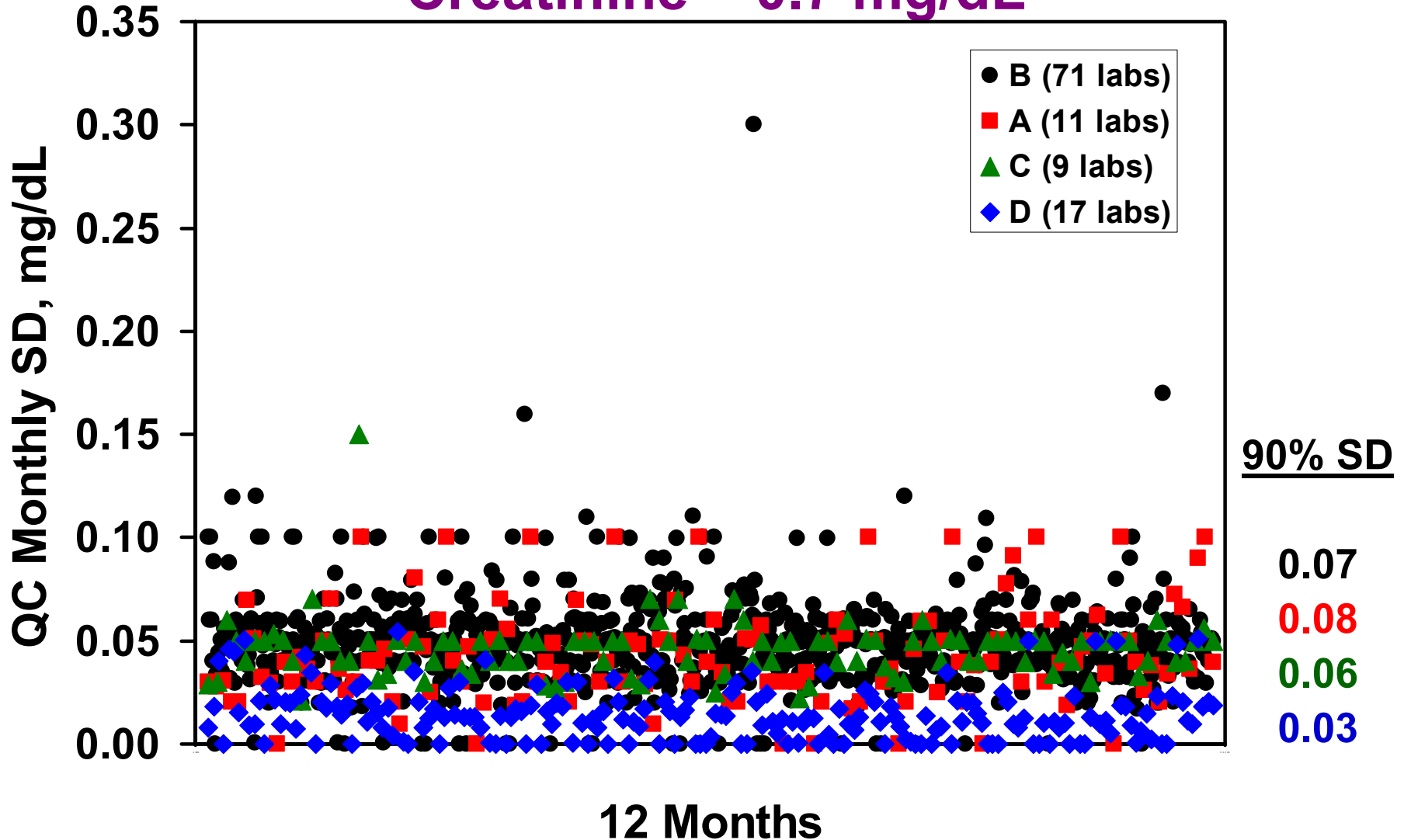
Certified value :  $74.57 \pm 0.57 \mu\text{mol}\cdot\text{L}^{-1}$  [ $U=k \cdot u_c$  ( $k=2$ )]



The averages of all results (based on all replicates measured) for each method when applied by more than 10 laboratories

# Bio-Rad inter-lab QC comparison (within-lab monthly SD for a single lot QC)\*

Creatinine ~ 0.7 mg/dL

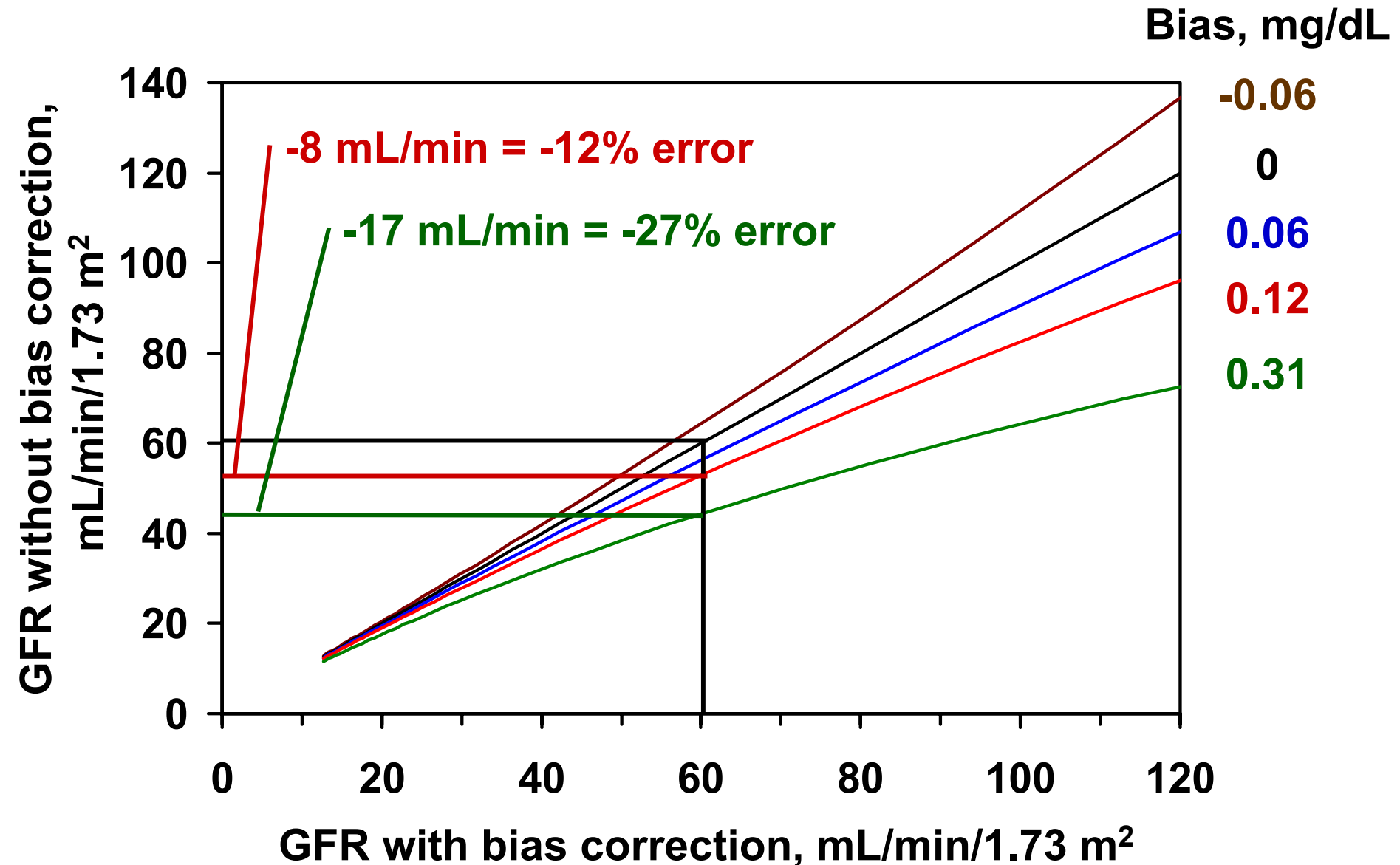


\* Bio-Rad Laboratories, Inc. Liquid Multiqual, 2002

# How does current performance impact calculated GFR

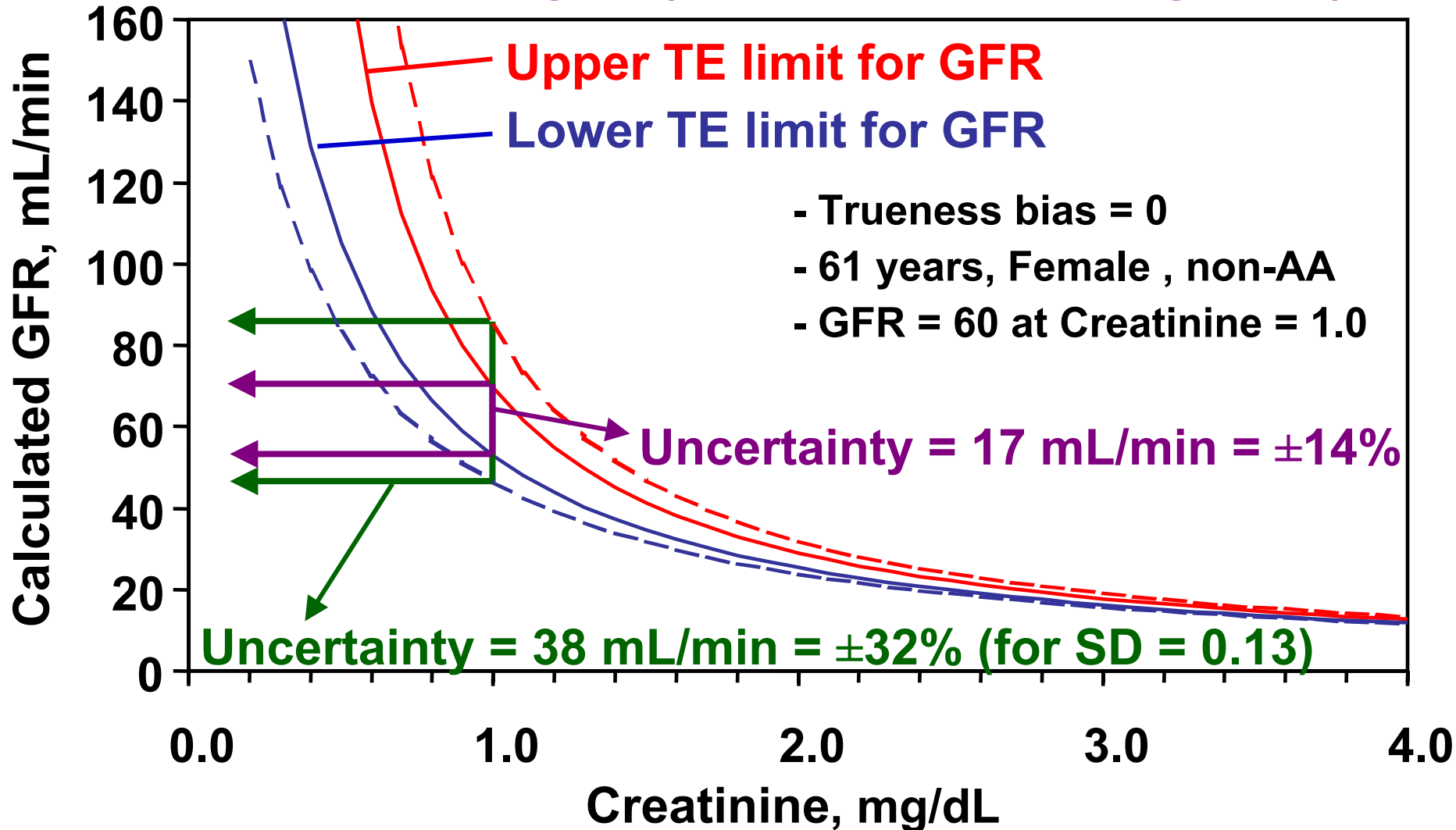
- **Four parameter MDRD equation**
- **Serum creatinine at GFR = 60 mL/min/1.73m<sup>2</sup> (adults)**
  - ▶ **1.0 mg/dL      60 Yr, F, not African-American**
  - ▶ **1.2 mg/dL      60 Yr, F, African-American**
  - ▶ **1.3 mg/dL      60 Yr, M, not African-American**
  - ▶ **1.5 mg/dL      60 Yr, M, African-American**

# Impact of creatinine bias on GFR



# Impact of method variability on GFR

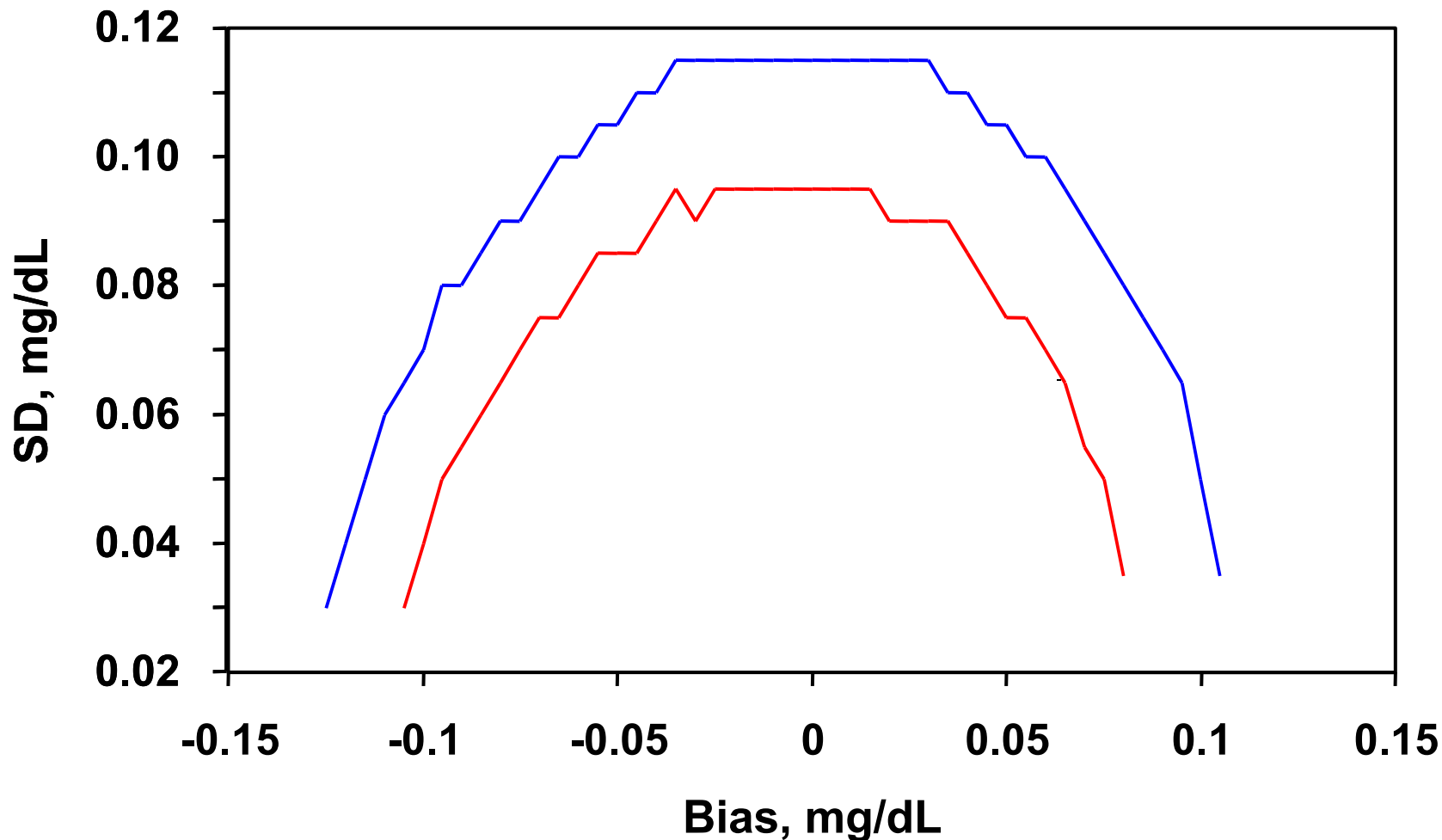
SD = 0.06 mg/dL (50%tile of CAP peer groups)



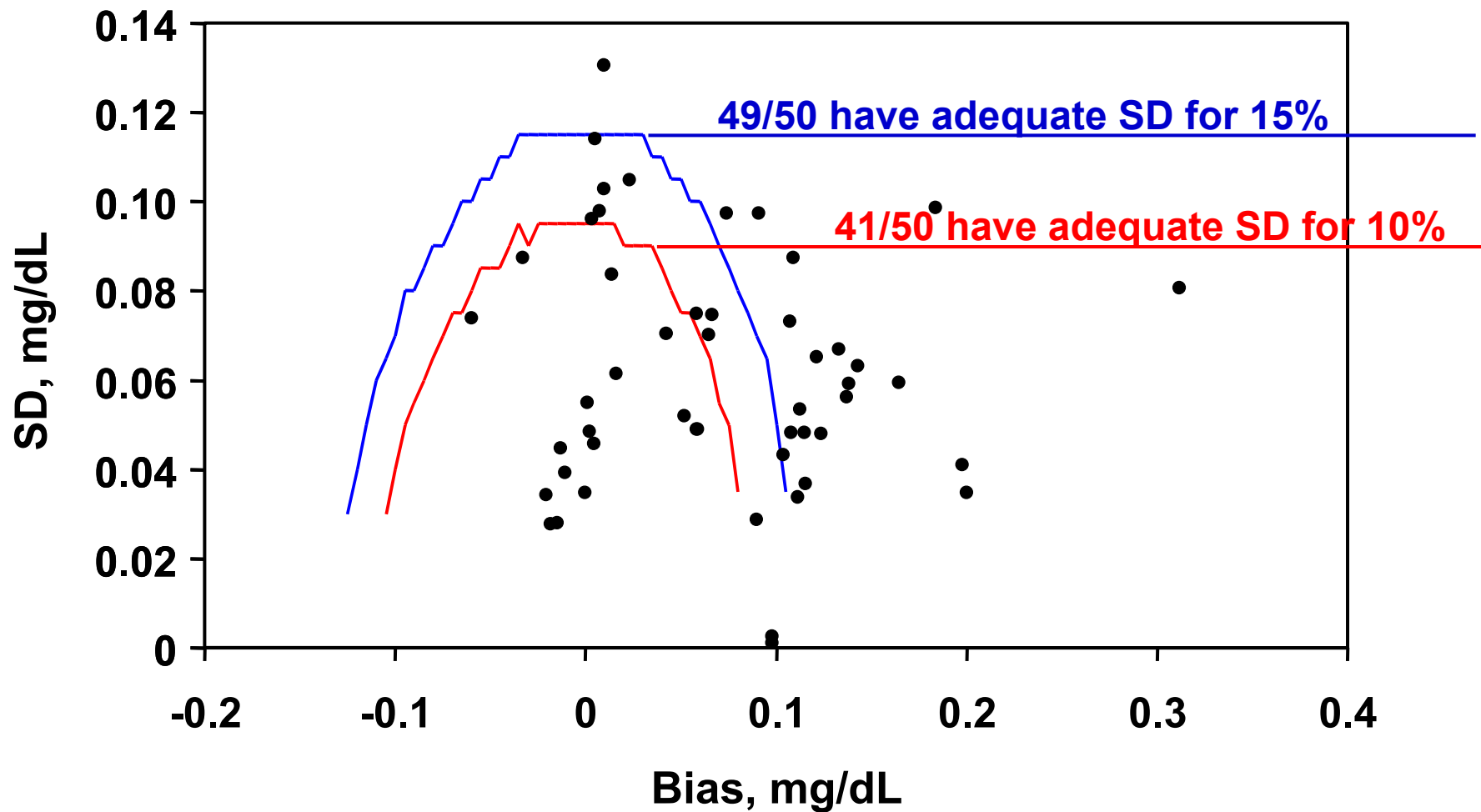


# What creatinine method performance is needed

- **Creatinine bias and SD should not increase the error in calculated GFR more than 10-15%**
- **Simulation using 491 patients in MDRD baseline group who had creatinine 1.0-1.5 mg/dL**
  - ▶ **Assume central lab (routine method) had zero bias, and SD = 0.03 mg/dL**
  - ▶ **Add bias and random error to the baseline creatinine values**
  - ▶ **Calculate increase in root mean squared error of the estimated GFR vs. the measured GFR**



Total error budget for creatinine measurement as a combination of biases and SDs that produce a relative increase of **less than 10% (red line)** or **less than 15% (blue line)** in the error when estimating GFR using the MDRD equation.



**Bias vs. a GC-IDMS RMP and inter-laboratory SD for 50 creatinine routine method peer groups for assay of a fresh frozen serum pool with creatinine 0.90 mg/dL in the 2003 CAP Comprehensive Chemistry Survey superimposed on the total error budget for creatinine measurement.**

# **Creatinine method non-specificity must also be addressed**

- **Alkaline Picrate**

- ▶ **Keto acids**
- ▶ **Glucose and other metabolites**
- ▶ **Proteins**
- ▶ **Drugs**

- **Enzymatic**

- ▶ **Drugs (fewer)**

# **Issues raised at the NKDEP Manufacturers' Forum in July 2004**

- **Global pressure for calibration traceability to IDMS (re-calibrate to remove bias)**
- **Need to coordinate method re-calibration with revised MDRD equation**
  - ▶ **Correction factors for creatinine are difficult to implement due to FDA labeling and potential for confusion among users**
  - ▶ **Timing of change and communication to users must be coordinated on a national/global scale**
- **Impact on PT grading**
  - ▶ **Bimodal distribution during transition**
  - ▶ **CAP agreed to support dual grading**
  - ▶ **Involve CMS in grading criteria during transition**
  - ▶ **Global PT/EQA impact**