Study Design and Results

Creatinine (Crea)

Clinical studies were conducted at two nursing homes in Florida and three physicians' offices in Illinois. The study involved 13 operators of the i-STAT CHEM8+ cartridge waived method (WM); three licensed practical nurses, two registered nurses, two certified nursing assistants, one certified nurse practitioner, one physician, one phlebotomist, one medical student, one administrator, and one economics student. None of the operators were given any training on how to perform the waived method, other than viewing the manufacturer's test instructions. Three sites had three operators and two sites had two operators.

Results of this testing were compared with results from the i-STAT CHEM8+ cartridge run by five trained laboratory professionals (one per site). To reduce variability, these measurements were repeated four times for each sample and the average (mean) value was used as the comparative method (CM) result. The CM was categorized as Type B according to FDA waiver application guidance[1].

Specimens were drawn by venipuncture into a 4 mL lithium heparin green-top specimen collection tube, and were used for both the WM and the CM.

The study was intended to demonstrate that after viewing only the manufacturer's test instructions, WM operators were able to obtain results that were accurate, as indicated by agreement with the CM.

The accuracy of the 362 reported patient results and 36 results from samples manipulated to targeted creatinine levels was assessed using the following two error zones[2].

The *Allowable Total Error (ATE) Zone* encompasses values that fall within the CM ± the greater of 0.3 mg/dL or 15%. The results of the study with respect to the ATE Zone follow:

Range of CM results (mg/dL)	Number of samples	Number of samples within ATE Zone	Percent of samples within ATE Zone
0.2 to 0.59	15	15	100
0.6 to 1.3	309	308	99.7
1.31 to 20.0	74	74	100
0.2 to 20.0	*398*	*397*	*99.7*

[1] *Draft Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications*. Food and Drug Administration (FDA), US Department of Health and Human Services, September 7, 2005.

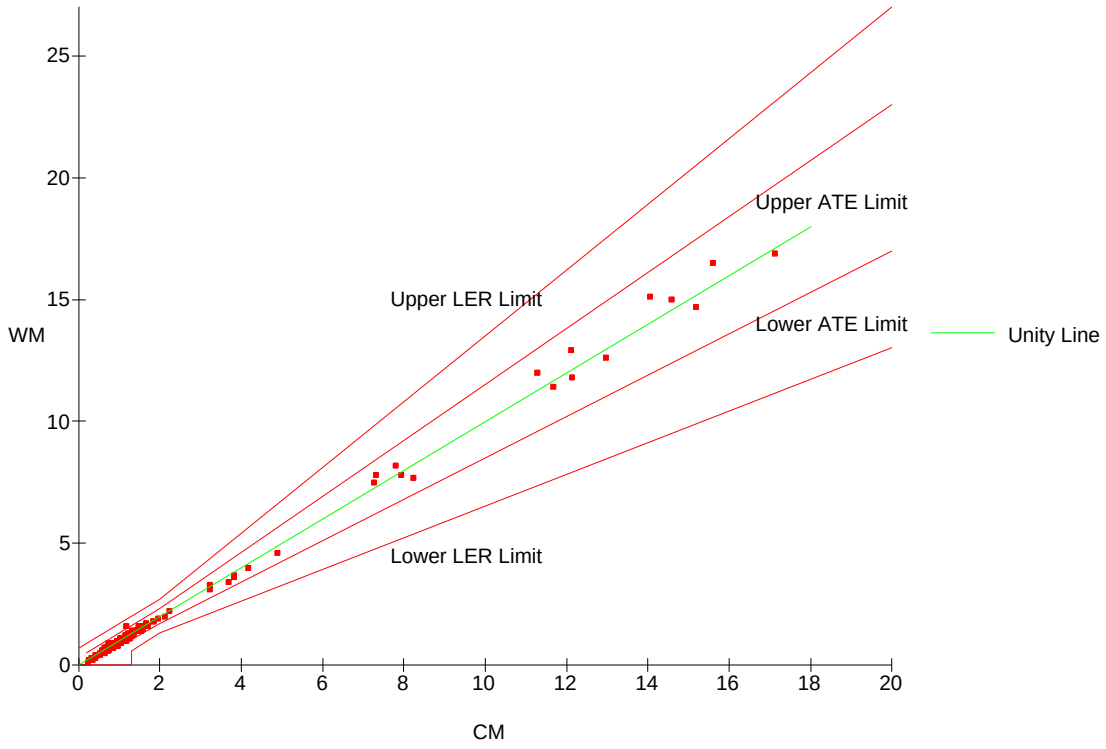
[2] *Draft Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications*. Food and Drug Administration (FDA), US Department of Health and Human Services, September 7, 2005.

The percentage of the samples over the entire range that fall within the ATE Zone was 99.7% (397/398), with a lower one-sided 95% exact confidence bound of 98.8%.

Values outside of the *Limits for Erroneous Results (LER)* are results for which "*potential harm can occur to the patients if these results are utilized in medical decision-making*"[3]. LER limits for creatinine (mg/dL) were as follows: +0.7 below 1.3, ±0.7 between 1.3-2.0, and ±35% above 2.0. In the study, all samples were within the LER limits (100% with a lower one-sided 95% exact confidence bound of 99.25%).

The scatter plot of the study results with ATE and LER limits is presented in the figure below:

Scatter Plot of WM vs. CM Creatinine Results (mg/dL), with ATE and LER Limits



[3] *Draft Guidance for Industry and FDA Staff: Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications*. Food and Drug Administration (FDA), US Department of Health and Human Services, September 7, 2005.

Descriptive statistics of the observed differences between WM and CM results are presented in the table below:

Range of CM results (mg/dL)	Average (mean) Difference	2.5th percentile of differences	97.5th percentile of differences
0.2 to 0.59	-0.028 mg/dL	-0.091 mg/dL	0.025 mg/dL
0.6 to 1.3	0.000 mg/dL	-0.10 mg/dL	0.10 mg/dL
1.31 to 20.0	0.3%	–6.3%	8.0%

The WM (y-axis) and CM (x-axis) results were compared by ordinary least squares regression analysis: the slope was 1.0174 with 95% confidence interval: 1.0119 to 1.0229; and the intercept was –0.021 with 95% confidence interval: –0.036 to –0.007. The systematic differences between WM and CM results estimated by regression analysis are presented in the table below:

CM (mg/dL)	Estimated systematic difference between WM and CM (mg/dL)
1.6	0.007