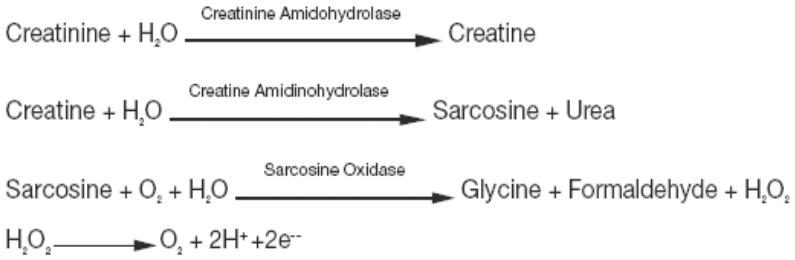
i-STAT Creatinine

Chemistry China Basin

Creatinine is measured amperometrically. Creatinine is hydrolyzed to creatine in a reaction catalyzed by the enzyme creatinine amidohydrolase. Creatine is then hydrolyzed to sarcosine in a reaction catalyzed by the enzyme creatine amidinohydrolase. The oxidation of sarcosine, catalyzed by the enzyme sarcosine oxidase, produces hydrogen peroxide (H2O2). The liberated hydrogen peroxide is oxidized at the platinum electrode to produce a current which is proportional to the sample creatinine concentration.



See below for information on factors affecting results. Certain substances, such as drugs, may affect analyte levels *in vivo*.1

If results appear inconsistent with the clinical assessment, the patient sample should be retested using another cartridge.

INTENDED USE

The test for creatinine, as part of the i-STAT System, is intended for use in the *in vitro* quantification of creatinine in arterial, venous, or capillary whole blood.

Contents

Each i-STAT cartridge contains one reference electrode (when potentiometric sensors are included in the cartridge configuration), sensors for the measurement of specific analytes, and a buffered aqueous calibrant solution that contains known concentrations of analytes and preservatives. For cartridges that contain a sensor for the measurement of creatinine, a list of reactive ingredients is indicated below:

Reactive Ingredient	Biological Source
Creatinine	N/A
Creatine Amidinohydrolase	*Actinobacillus sp.*
Creatinine Amidohydrolase	Microbial
Sarcosine Oxidase	Microbial

Metrological Traceability

The i-STAT System test for creatinine measures creatinine amount-of-substance concentration in the plasma fraction of arterial, venous, or capillary whole blood

(dimension µmol L-1) for *in vitro* diagnostic use. Creatinine values assigned to i-STAT's controls and calibration verification materials are traceable to the U.S. National Institute of Standards and Technology (NIST) standard reference material SRM909.

i-STAT System controls and calibration verification materials are validated for use only with the i-STAT System and assigned values may not be commutable with other methods. Further information regarding metrological traceability is available from Abbott Point of Care Inc..

Expected Values

Test/Abbreviation	Units*	Reportable Range	Reference Range
Creatinine/Crea	mg/dL	0.2 – 20.0	0.6 – 1.3[2]
	µmol/L	18 – 1768	53 – 115

To convert a creatinine result from mg/dL to mol/L, multiply the mg/dL value by 88.4.

The i-STAT reference ranges for whole blood listed above are similar to reference ranges derived from serum or plasma measurements with standard laboratory methods.

The reference range programmed into the analyzer and shown above is intended to be used as a guide for the interpretation of results. Since reference ranges may vary with demographic factors such as age, gender and heritage, it is recommended that reference ranges be determined for the population being tested.

* The i-STAT System can be configured with the preferred units.

Clinical Significance

Elevated levels of creatinine are mainly associated with abnormal renal function and occur whenever there is a significant reduction in glomerular filtration rate or when urine elimination is obstructed. The concentration of creatinine is a better indicator of renal function than urea or uric acid because it is not affected by diet, exercise, or hormones.

The creatinine level has been used in combination with BUN to differentiate between prerenal and renal causes of an elevated urea/BUN.

Performance Characteristics

The typical performance data summarized below were collected in health care facilities by professionals trained in the use of the i-STAT System and comparative methods. Clinical settings vary and some may require different performance characteristics to assess renal function status than others (e.g., medication dosing, intravenous contrast use, and outpatient clinic). If deemed necessary by a health care facility, performance data should be obtained in specific clinical settings to assure patients' needs are met.

Precision data were collected in multiple sites as follows3: Duplicates of each control fluid were tested in the morning and in the afternoon on five days for a total of 20 replicates. The averaged statistics are presented below.

Method comparison data were collected using CLSI guideline EP9-A4. Venous blood samples, collected in lithium or sodium heparin Vacutainer® tubes, and arterial blood samples, collected in blood gas syringes, were analyzed in duplicate on the i-STAT System. A portion of each specimen was centrifuged, and the separated plasma was analyzed on the comparative method.

Deming regression analysis5 was performed on the first replicate of each sample. In the method comparison table, n is the number of specimens in the data set, Sxx and Syy refer to the estimates of imprecision based on the duplicates of the comparative and the i-STAT methods respectively, Sy.x is the standard error of the estimate, and r is the correlation coefficient.*

Interference studies were based on CLSI guideline EP7.[6]

*The usual warning relating to the use of regression analysis is summarized here as a reminder: For any analyte, "if the data is collected over a narrow range, the estimate of the regression parameters are relatively imprecise and may be biased. Therefore, predictions made from these estimates may be invalid".[5] The correlation coefficient, r, can be used as a guide to assess the adequacy of the comparative method range in overcoming this problem. As a guide, the range of data can be considered adequate if r>0.975.

Precision Date (mg/dL)

Aqueous Control	Mean	SD	%CV
Level 1	4.7	0.08	1.7
Level 3	0.76	0.05	6.3

Method Comparison (mg/dL)

	Roche Integra 800	Beckman LX20	J & J Vitros 950	Dade Dimension RxL
n	30	58	31	36
Sxx	0.029	0.141	0.04	0.04
Syy	0.112	0.143	0.12	0.06
Slope	0.929	0.960	0.948	0.964
Int't	0.237	0.022	0.206	0.100
Syx	0.204	0.261	0.165	0.123
Xmin	0.4	0.7	0.5	0.5
Xmax	10.3	20.0	7.2	5.7
r	0.997	0.996	0.991	0.986

Cartridge Comparison

The performance characteristics of the sensors are equivalent in all cartridge configurations. System difference analysis was performed on 39 patient samples using the i-STAT CHEM8+ and i-STAT Crea cartridges. In the 0.42-2.50 mg/dL range, the average difference was -0.01. In the 2.50-9.08 mg/dL range, the average difference was -0.04.

Factors Affecting Results*

Interferent	Effect
Acetaminophen	Creatinine results will increase by approximately 0.25 mg/dL (22 µmol/L) per every 1 mmol/L of acetaminophen.
Ascorbate	0.227 mmol/L ascorbate will cause a 0.7 mg/dL (62 mol/L) increase in creatinine.
Bromide	100 mg/dL (12.5 mmol/L) bromide will increase creatinine by 0.8 mg/dL (71 mol/L) from an initial creatinine concentration of 1.0 mg/dL (88 mol/L).
CO2	For Crea values below 2 mg/dL: For ***P***CO_2 values above 40 mmHg, the values are increased by 6.9% for every 10 mmHg For ***P***CO_2 values below 40 mmHg, the values are decreased by 6.9% for every 10 mmHg [Cr]corrected = [Cr]istat X { 1 - (0.069 X [(***P***CO_2 -40)/10]) } For Crea values above 2 mg/dL: For ***P***CO_2 values above 40, the values are decreased by 3.7% for every 10 mmHg For ***P***CO_2 values below 40, the values are increased by 3.7% for every 10 mmHg Cr]corrected = [Cr]istat X { 1 - (0.037 X [(40 - ***P***CO_2)/10]) }
Creatine	5 mg/dL (382 mol/L) creatine will cause a 0.20 mg/dL (18 mol/L) increase in Creatinine. For clinical situations in which creatine may be elevated, see note (1) below.

Interferent	Effect
N-acetylcysteine	16.6 mmol/L N-acetylcysteine will cause a 0.4 mg/dL (36 µmol/L) increase in creatinine.
Hydroxyurea (Droxia®, Hydrea®)	Hydroxyurea may cause significant errors in the measurement of creatinine with the i-STAT System. Use an alternative method to measure creatinine when patients have been administered hydroxyurea. See note (2) below for typical uses of this drug and note (3) below for details of the interference.

Notes:

(1) The normal range of creatine concentration in plasma is 0.17–0.70 mg/dL (13 – 53 mol/L) in males and 0.35 – 0.93 mg/dL (27 – 71 mol/L) in females7. Creatine may be elevated in patients using creatine supplements, experiencing muscle trauma or other primary or secondary myopathies, taking statins for hyperlipidemia control, or in patients with hyperthyroidism or a rare genetic defect of the creatine transporter protein.

(2) Hydroxyurea is a DNA synthesis inhibitor used in the treatment of various forms of cancer, sickle cell anemia, and HIV infection. This drug is used to treat malignancies including melanoma, metastatic ovarian cancer, and chronic myelogenous leukemia. It is also used in the treatment of polycythemia vera,

thrombocytopenia, and psoriasis. At typical doses ranging from 500 mg to 2 g/day, concentrations of hydroxyurea in patients' blood may be sustained at approximately 100 to 500 mol/L. Higher concentrations may be observed soon after dosing or at higher therapeutic doses.

(3) For every 100 mol/L hydroxyurea in the whole blood sample, creatinine will be increased by approximately 1.85 mg/dL (164 mol/L), up to a whole blood hydroxyurea concentration of at least 921 mol/L (maximum concentration tested). The magnitude of the bias is independent of the creatinine level over a range of at least 1.0 mg/dL (88 mol/L) to 12.4 mg/dL (1096 mol/L).

Bicarbonate up to 40 mmol/L, bilirubin up to 20 mg/dL (342 mol/L), calcium up to 5.0 mg/dL (1.25 mmol/L), dopamine up to 13 mg/dL (0.85 mmol/L), methyldopa up to 2.5 mg/dL (118.4 mol/L), salicylate up to 77.5 mg/dL (4.34 mmol/L), sarcosine up to 1.0 mmol/L, and uric acid up to 20 mg/dL (1190 mol/L) were tested and found not to interfere with creatinine results.

*It is possible that other interfering substance may be encountered. These results are representative and your results may differ somewhat due to test-to-test variation. The degree of interference at concentrations other than those listed might not be predictabl

References

1. D. S. Young, Effects of Drugs on Clinical Laboratory Tests, 3rd ed. (Washington, DC: American Association of Clinical Chemistry, 1990).
2. B. E. Statland, Clinical Decision Levels for Lab Tests, 2nd ed. (Oradell, NJ: Medical Economics Company, Inc., 1987).
3. CLSI. *Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline.* CLSI document EP5-A [ISBN 1-56238-368-X]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 1999.
4. CLSI. *Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline.* CLSI document EP9-A [ISBN 1-56238-283-7]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898, USA 1995.
5. P.J. Cornbleet and N. Gochman, "Incorrect Least-Squares Regression Coefficients in Method Comparison Analysis," Clinical Chemistry 25:3, 432 (1979).
6. CLSI. *Interference Testing in Clinical Chemistry; Proposed Guideline.* CLSI document EP7-P (ISBN 1-56238-020-6). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087, 1986.
7. Tietz Textbook of Clinical Chemistry 3rd Edition, CA Burtis and ER Ashwood, ed., WB Saunders Company, 1999, page 1808.