VITROS Products Chemistry

INSTRUCTIONS FOR USE

UREA-CREA

VITROS XT Chemistry Products UREA-CREA Slides

Urea/Creatinine

REF 684 4294

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UREA Test

Urea

Rx ONLY

Intended Use

For *in vitro* diagnostic use only.

The UREA test within the VITROS XT Chemistry Products UREA-CREA Slides quantitatively measures urea concentration, reported either as urea nitrogen or as urea (UREA), in serum, plasma, and urine using VITROS XT 7600 Integrated Systems. Measurements obtained by this device are used in the diagnosis and treatment of certain renal and metabolic diseases.

Summary and Explanation of the Test

The major pathway of nitrogen excretion is in the form of urea that is synthesized in the liver, released into the blood, and cleared by the kidneys. A high serum urea nitrogen occurs in glomerulonephritis, shock, urinary tract obstruction, pyelonephritis, and other causes of acute and chronic renal failure. Severe congestive heart failure, hyperalimentation, diabetic ketoacidosis, dehydration, and bleeding from the gastrointestinal tract elevate urea nitrogen. Low urea nitrogen often occurs in normal pregnancy, with decreased protein intake, in acute liver failure, and with intravenous fluid administration.[1]

Principles of the Procedure

The UREA test is a multilayered, analytical element coated on a polyester support.

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. Water and nonproteinaceous components then travel to the underlying reagent layer, where the urease reaction generates ammonia. The semipermeable membrane allows only ammonia to pass through to the color-forming layer, where it reacts with the indicator to form a dye.

The reflection density of the dye is measured and is proportional to the concentration of urea in the sample.

Test Type and Conditions

Test Type	VITROS System*	Approximate Incubation Time	Temperature	Wavelength	Reaction Sample Volume
Colorimetric	XT 7600	5 minutes	37 °C (98.6 °F)	670 nm	4.3 µL

* Not all products and systems are available in all countries.

Reaction Scheme

$H_2NCONH_2 + H_2O \xrightarrow{\text{urease}} 2NH_3 + CO_2$

NH_3 + ammonia indicator → dye

Warnings and Precautions

For *in vitro* diagnostic use only.

WARNING: Take care when handling materials and samples of human origin. Since no test method can offer complete assurance that infectious agents are absent, consider all clinical specimens, controls, and calibrators potentially infectious. Handle specimens, solid and liquid waste, and test components in accordance with local regulations and CLSI Guideline M29[2] or other published biohazard safety guidelines.

For specific warnings and precautions for calibrators, quality control materials, and other components, refer to the Instructions for Use for the appropriate VITROS product, or to other manufacturer's product literature.

Reagents

Slide Ingredients

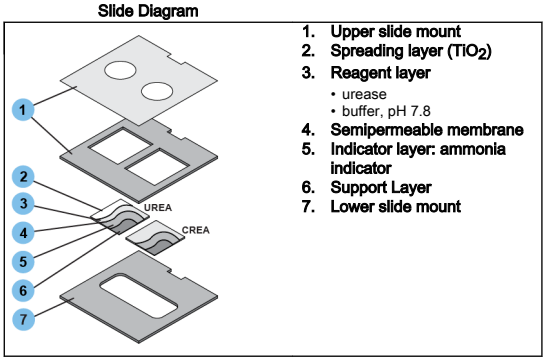
Reactive Ingredients per cm²

Urease (jack bean) 1.2 U and N-propyl-4-(2,6-dinitro-4-chlorobenzyl)-quinolonium ethane sulfonate (ammonia indicator) 0.26 mg.

Other Ingredients

Pigment, binders, buffer, surfactants, stabilizers, chelator and cross-linking agent

Slide Diagram



1. Upper slide mount
2. Spreading layer (TiO_2)
3. Reagent layer
   - urease
   - buffer, pH 7.8
4. Semipermeable membrane
5. Indicator layer: ammonia indicator
6. Support Layer
7. Lower slide mount

Reagent Handling

Caution: Do not use slide cartridges with damaged or incompletely sealed packaging.

- Inspect the packaging for signs of damage.
- Be careful when opening the outer packaging with a sharp instrument so as to avoid damage to the individual product packaging.

Reagent Preparation

IMPORTANT: The slide cartridge must reach room temperature, 18–28 °C (64–82 °F), before it is unwrapped and loaded into the slide supply.

1. Remove the slide cartridges from storage.
2. Warm the wrapped cartridge at room temperature for 30 minutes when taken from the refrigerator or 60 minutes from the freezer.
3. Unwrap and load the cartridge into the slide supply.

Note: Load the cartridges within 24 hours after they reach room temperature, 18–28 °C (64–82 °F).

Reagent Storage and Stability

VITROS XT UREA-CREA Slides are stable until the expiration date on the carton when they are stored and handled as specified. Do not use beyond the expiration date.

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	≤ 4 weeks
	Frozen	≤ -18 °C (≤ 0 °F)	Until expiration date
Opened	On-analyzer	System turned on	≤ 2 weeks
	On-analyzer	System turned off	≤ 2 hours

- Do not store with or near ammonia, ammonia compounds, or amines.
- Verify performance with quality control materials:
  - If the system is turned off for more than 2 hours.
  - After reloading cartridges that have been removed from the slide supply and stored for later use.

Specimen Collection, Preparation and Storage

Specimens Recommended

- Serum
- Plasma: Heparin (lithium and sodium)
- Urine

IMPORTANT: Certain collection devices have been reported to affect other analytes and tests.[3] Owing to the variety of specimen collection devices available, Ortho Clinical

	Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.

Specimens Not Recommended

- Plasma[4] : Sodium fluoride (Fluoride inhibits the enzyme urease.)
- Urine:
  - Glacial acetic acid as a preservative
  - Concentrated hydrochloric acid as a preservative
  - Boric acid (in any form) as a preservative

Serum and Plasma

Specimen Collection and Preparation

Collect specimens using standard laboratory procedures.[5,6]

Note:	For details on minimum fill volume requirements, refer to the operating instructions for your system.

Patient Preparation

No special patient preparation is necessary.

Special Precautions

Centrifuge serum and plasma specimens and remove the serum or plasma from the cellular material within 4 hours of collection.[4]

Specimen Handling and Storage

- Handle and store specimens in stoppered containers to avoid contamination and evaporation.
- Mix samples by gentle inversion and bring to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Specimen Storage and Stability: Serum and Plasma

Storage	Temperature	Stability
Room temperature	18–28 °C (64–82 °F)	≤ 1 day
Refrigerated	2–8 °C (36–46 °F)	≤ 5 days
Frozen	≤ -18 °C (≤ 0 °F)	≤ 30 days

Urine

Specimen Collection and Preparation

- Collect specimens using standard laboratory procedures.[7]
- Keep urine specimens refrigerated until analysis.

Note:	For details on minimum fill volume requirements, refer to the operating instructions for your system.

Patient Preparation

No special patient preparation is necessary.

Special Precautions

Urine specimens must be pretreated prior to processing. Refer to “Specimen Pretreatment” for instructions.

Specimen Handling and Storage

- Handle and store specimens in stoppered containers to avoid contamination and evaporation.
- Mix samples by gentle inversion and bring to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Specimen Storage and Stability: Urine

Storage	Temperature	Stability
Room temperature	18–28 °C (64–82 °F)	≤ 5 days
Refrigerated	2–8 °C (36–46 °F)	≤ 7 days
Frozen	≤ -18 °C (≤ 0 °F)	≤ 6 months

Specimen Pretreatment

Urine

Predilution

Pretreatment is managed by the analyzer, no operator intervention is required.

Testing Procedure

Materials Provided

VITROS XT Chemistry Products UREA-CREA Slides

Materials Required but Not Provided

- VITROS Chemistry Products Calibrator Kit 1
- Quality control materials, such as VITROS Chemistry Products Performance Verifier I and II for serum and plasma
- VITROS Chemistry Products 7% BSA
- Isotonic saline or reagent-grade water
- VITROS Chemistry Products FS Diluent Pack 2 (BSA/Saline) (for on-analyzer dilution of serum and plasma samples)
- VITROS Chemistry Products FS Diluent Pack 3 (Specialty Diluent/Water) (for on-analyzer dilution of urine samples)

Operating Instructions

- Check reagent inventories at least daily to ensure that quantities are sufficient for the planned workload.
- For additional information, refer to the operating instructions for your system.

IMPORTANT:	Bring all fluids and samples to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Sample Dilution

Serum and Plasma

If urea nitrogen concentrations exceed the system's measuring (reportable or dynamic) range:

On-Analyzer Sample Dilution

Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure. For VITROS XT 7600 Integrated Systems, use VITROS Chemistry Products FS Diluent Pack 2 for the dilution.

Manual Sample Dilution

1. Dilute the sample with 1 part sample and 1 part VITROS 7% BSA.
2. Reanalyze.
3. Multiply the results by 2 to obtain an estimate of the original sample's urea nitrogen concentration.

Urine

If urea nitrogen concentrations exceed the system's measuring (reportable or dynamic) range:

On-Analyzer Sample Dilution

Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure. For VITROS XT 7600 Integrated Systems, use VITROS Chemistry Products FS Diluent Pack 3 for the dilution.

Manual Sample Dilution

1. Dilute the sample with 1 part sample and 1 part isotonic saline or reagent-grade water.
2. Reanalyze.
3. Multiply the results by 2 to obtain an estimate of the original sample's urea nitrogen concentration.

Calibration

Required Calibrators

VITROS Chemistry Products Calibrator Kit 1

Note:	The same VITROS Calibrator Kit is used to calibrate serum, plasma, and urine. However, specific supplementary assigned values (SAVs) are applied for each body fluid.

Calibrator Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Calibrator Kit 1.

Note: After reconstituting calibrators, do not dilute further when calibrating for urine.

Calibration Procedure

Refer to the operating instructions for your system.

When to Calibrate

Calibrate:

- When the slide lot number changes.
- When critical system parts are replaced due to service or maintenance.
- When government regulations require.
  For example, in the USA, CLIA regulations require calibration or calibration verification at least once every six months.

The UREA test within the VITROS XT UREA-CREA Slides may also need to be calibrated:

- If quality control results are consistently outside acceptable range.
- After certain service procedures have been performed.

For additional information, refer to the operating instructions for your system.

Calculations

Reflectance from the slide is measured at 670 nm after the fixed incubation time. Once a calibration has been performed for each slide lot, urea nitrogen concentration in unknown samples can be determined using the software-resident endpoint colorimetric math model and the response obtained from each unknown test slide.

Validity of a Calibration

Calibration parameters are automatically assessed by the system against a set of quality parameters detailed in Review Assay Data screen on VITROS XT Integrated Systems. Failure to meet any of the pre-defined quality parameters results in a failed calibration. The calibration report should be used in conjunction with quality control results to determine the validity of a calibration.

Measuring (Reportable or Dynamic) Range

Fluid	Conventional Units (mg/dL urea N)	SI Units (mmol/L urea)	Alternate Units (mg/dL urea)
Serum/Plasma	2.0–120.0	0.71–42.83	4.29–257.40
Urine*	67–2520	23.91–899.39	143.72–5405.40

* After multiplying by a 21x dilution factor.

For out-of-range samples, refer to “Sample Dilution.”

Traceability of Calibration

The Values assigned to the VITROS Chemistry Products Calibrator Kit 1 for UREA are traceable to a CDC Urease/GLDH comparative method[8] and National Institute of Standards and Technology (NIST) SRM® 912 urea standard reference material.

Quality Control

Quality Control Material Selection

IMPORTANT: VITROS Performance Verifiers are recommended for use with VITROS XT Integrated Systems. Evaluate the performance of other commercial control fluids for compatibility with this test before using for quality control.

- Control materials other than VITROS Performance Verifiers may show a difference when compared with other urea nitrogen methods if they:
  - Depart from a true human matrix.
  - Contain high concentrations of preservatives, stabilizers, or other nonphysiological additives.
- Do not use control materials stabilized with ethylene glycol.

Serum

- Some controls that are low in pH may show a negative bias that may be avoided by reconstituting lyophilates with a bicarbonate diluent instead of with water. [9]

- Proficiency survey samples may show a negative bias similar to controls low in pH. Contact the testing agency for instructions because reconstituting with special diluents may affect other analyte values (e.g., reconstituting with sodium bicarbonate will affect sodium proficiency scores).[10]
- Ammonium bicarbonate diluent should not be used as it will cause a positive bias in test results.

Urine

For urine specimens, use commercially available urine control materials.

IMPORTANT: If using a VITROS XT Integrated Systems in On-Analyzer Dilution Mode, do not manually dilute samples for analysis and do not multiply by a dilution factor after analysis. Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure.

Quality Control Procedure Recommendations

- Choose control levels that check the clinically relevant range.
- Analyze quality control materials in the same manner as patient samples, before or during patient sample processing.
- To verify system performance, analyze control materials:
  - After calibration.
  - According to local regulations or at least once each day that the test is being performed.
  - After specified service procedures are performed. Refer to the operating instructions for your system.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- For general quality control recommendations, refer to *Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline-Fourth Edition* [11]or other published guidelines.
- For additional information, refer to the operating instructions for your system.

Quality Control Material Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Chemistry Products Performance Verifier I and II or to other manufacturer's product literature.

Results

Reporting Units and Unit Conversion

The VITROS XT Systems may be programmed to report UREA results in conventional, SI, and alternate units.

Conventional Units	SI Units	Alternate Units
mg/dL urea N	mmol/L urea (mg/dL urea N x 0.3569)	mg/dL urea (mg/dL urea N x 2.145)

Limitations of the Procedure

Known Interferences

Ammonium ions may cause an increase in measured UREA value equivalent to the specimen's nitrogen content.[12]

Serum and Plasma

The VITROS XT Chemistry Products UREA-CREA Slides method was screened for interfering substances following CLSI EP07.[13,14] The substances listed in the table, when tested at the concentrations indicated, caused the bias shown.
For substances that were tested and did not interfere, refer to "Specificity."

	Interferent Concentration		Urea nitrogen Concentration		Bias**	
Interferent*	Conv. Units	SI Units	Conv. Units (mg/dL)	SI Units (mmol/L)	Conv. Units (mg/dL)	SI Units (mmol/L)
Total protein	12 g/dL	120 g/L	37	13	-4.3	-1.5

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

** The bias is an estimate of the maximum bias observed.

Other Limitations

Certain drugs and clinical conditions are known to alter UREA concentrations *in vivo*. For additional information, refer to one of the published summaries.[15,16]

Expected Values

Reference Interval

The serum reference interval is the central 95% of results from an internal study of 3160 apparently healthy adults from a working population (612 females and 2548 males).

The urine reference interval is based on an external study.[17]

	Conventional Units (mg/dL urea N)	SI Units (mmol/L urea)	Alternate Units (mg/dL urea)
Serum			
Male	9–20	3.2–7.1	19–43
Female	7–17	2.5–6.1	15–36
Urine			
24–hour	12–20 g/day*	428–714 mmol/day**	26–43 g/day*

* Urea nitrogen concentration (mg/dL) x 24-hour volume (dL) = mg/day. To convert mg/day to g/day, divide by 1000.

** Urea nitrogen concentration (mmol/L) x 24-hour volume (L) = mmol/day.

Each laboratory should confirm the validity of these intervals for the population it serves.

Performance Characteristics

Detection Capability

The Limit of Quantitation (LoQ) for the UREA test within the VITROS XT UREA-CREA Slides is 2.0 mg/dL for serum/plasma and 67 mg/dL for urine. The total number of LoQ determinations was 72. The LoQ was established consistent with CLSI EP17.[18]

Fluid Type	LoQ*	
	Conventional Units (mg/dL Urea N)	SI Units (mmol/L)
Serum/Plasma	2.0	0.71
Urine	67	23.91

* The Total Error goal used to accept the LoQ was ≤ 1.2 mg/dL for serum and ≤ 21 mg/dL Urea N for urine.

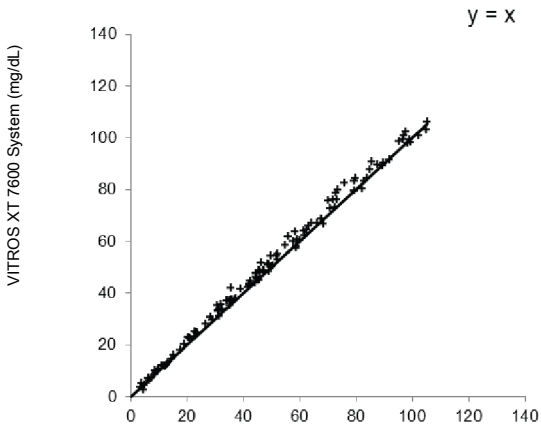
Method Comparison

The plots and tables below show the results of a method comparison study with serum samples and urine samples analyzed on the VITROS XT 7600 Integrated System and with the Urease/GLDH comparative method.[8]

The tables also show the results of comparisons with serum and urine samples between the VITROS XT 7600 Integrated System and the VITROS Chemistry Products BUN/UREA Slides on a VITROS 5600 Integrated System. Testing followed CLSI EP09.[19]

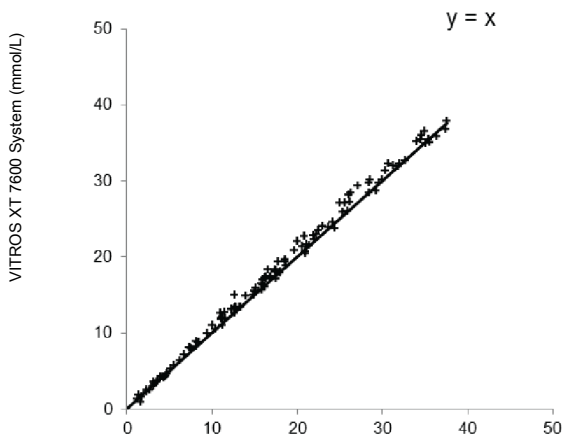
Serum

Conventional Units



Comparative Method: Urease/GLDH (mg/dL)

SI Units



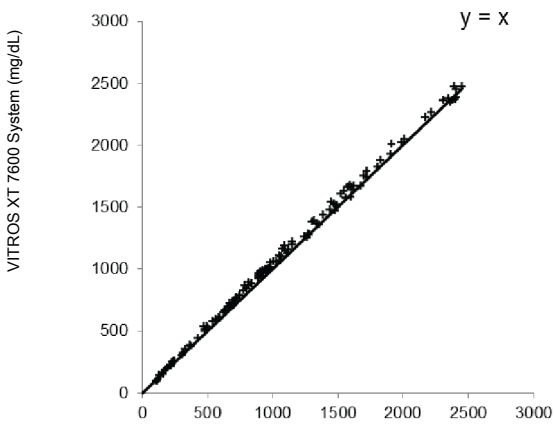
Comparative Method: Urease/GLDH (mmol/L)

				Conventional Units (mg/dL urea N)			SI Units (mmol/L urea)		
	n	Slope	Correlation Coefficient	Range of Sample Conc.	Intercept	Sy.x	Range of Sample Conc.	Intercept	Sy.x
XT 7600 vs. Comparative Method	124	1.05	0.998	3–105	-0.43	1.84	1.2–37.6	-0.15	0.66
XT 7600 vs. 5600†	124	1.04	0.999	3–106	0.00	1.20	0.9–37.8	0.07	0.45

† Comparisons made using the same patient samples tested with the VITROS Chemistry Products BUN/UREA Slides run on the VITROS 5600 Integrated System.

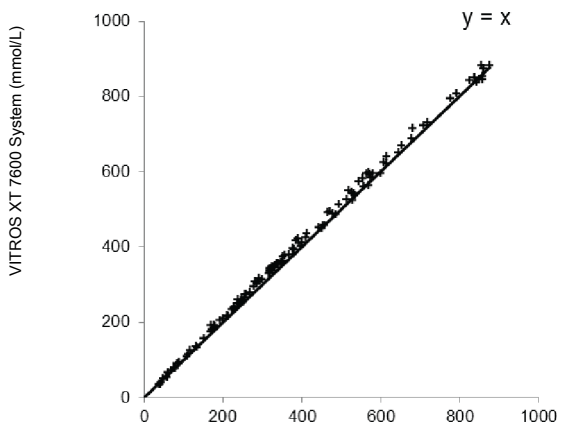
Urine

Conventional Units



Comparative Method: Urease/GLDH (mg/dL)

SI Units



Comparative Method: Urease/GLDH (mmol/L)

	n	Slope	Correlation Coefficient	Conventional Units (mg/dL urea N) Range of Sample Conc.	Intercept	Sy.x	SI Units (mmol/L urea) Range of Sample Conc.	Intercept	Sy.x
XT 7600 vs. Comparative Method	128	1.05	0.999	106–2456	-7.35	27.37	37.8 –876.6	-2.62	9.77
XT 7600 vs. 5600†	128	1.05	0.999	105–2451	-13.21	23.73	38.0 –892.1	-4.55	11.05

† Comparisons made using the same patient samples tested with the VITROS Chemistry Products BUN/UREA Slides run on the VITROS 5600 Integrated System.

Precision

Precision was evaluated with patient pools and quality control materials on the VITROS XT 7600 Integrated System following CLSI EP05 .[20] The data presented are a representation of test performance and are provided as a guideline. Variables such as sample handling and storage, reagent handling and storage, laboratory environment and system maintenance can affect reproducibility of test results.

Serum

System	Conventional Units (mg/dL urea N) Mean Concentration	Repeatability* SD	Repeatability* CV %	Within Day** SD	Within Day** CV %	Within Lab*** SD	Within Lab*** CV %	No. of Obs.	No. of Days
XT 7600	3	0.1	4.0	0.2	8.0	0.2	8.7	80	20
	10	0.1	1.0	0.2	1.8	0.2	2.1	80	20
	11	0.1	1.2	0.2	2.1	0.2	2.1	80	20
	17	0.3	1.6	0.3	1.9	0.3	1.9	80	20
	51	0.7	1.3	0.7	1.3	0.8	1.5	80	20
	107	1.1	1.0	1.2	1.2	1.4	1.3	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

System	SI Units (mmol/L urea) Mean Concentration	Repeatability* SD	Repeatability* CV %	Within Day** SD	Within Day** CV %	Within Lab*** SD	Within Lab*** CV %	No. of Obs.	No. of Days
XT 7600	1.0	0.04	4.1	0.08	8.0	0.08	8.7	80	20
	3.5	0.04	1.0	0.06	1.8	0.07	2.1	80	20
	4.0	0.05	1.2	0.08	2.1	0.08	2.1	80	20
	6.1	0.10	1.6	0.11	1.8	0.11	1.8	80	20
	18.1	0.24	1.3	0.24	1.3	0.28	1.5	80	20
	38.3	0.39	1.0	0.45	1.2	0.51	1.3	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

Urine

System	Conventional Units (mg/dL urea N)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	84	2.4	2.8	6.0	7.1	7.2	8.5	80	20
	293	3.8	1.3	5.4	1.8	6.8	2.3	80	20
	404	4.1	1.0	7.1	1.8	9.1	2.3	80	20
	683	7.6	1.1	7.6	1.1	12.2	1.8	80	20
	1453	14.0	1.0	19.5	1.3	19.5	1.3	80	20
	2331	21.4	0.9	28.2	1.2	30.6	1.3	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

System	SI Units (mmol/L urea)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	30.0	0.85	2.8	2.13	7.1	2.55	8.5	80	20
	104.6	1.36	1.3	1.92	1.8	2.44	2.3	80	20
	144.1	1.47	1.0	2.53	1.8	3.25	2.3	80	20
	243.9	2.70	1.1	2.73	1.1	4.35	1.8	80	20
	518.4	5.00	1.0	6.95	1.3	6.95	1.3	80	20
	832.1	7.65	0.9	10.06	1.2	10.93	1.3	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

Specificity

Substances that Do Not Interfere

Serum and Plasma

The substances listed in the table below were tested with the UREA test within VITROS XT UREA-CREA Slides following CLSI EP07[13,14] and found not to interfere, bias < 2.0 mg/dL (< 0.7 mmol/L) at 9 mg/dL (3.2 mmol/L) urea N and bias < 4.0 mg/dL (< 1.4 mmol/L) at 40 mg/dL (14.3 mmol/L) urea N at the concentration shown.

Compound	Concentration		Compound	Concentration	
5-Aminosalicylic acid	2.04 mg/dL	133 µmol/L	Hypaque (diatrizoate)	19.28 mg/dL	314 µmol/L
6-mercaptopurine	0.2 mg/dL	13.1 µmol/L	Ibuprofen	50 mg/dL	2425 µmol/L
Acetaminophen	20 mg/dL	1324 µmol/L	Insulin	3.12 µg/dL	5.38 nmol/L
Alprazolam	0.2 mg/dL	6.48 µmol/L	Intralipid	2000 mg/dL	20 g/L
Amikacin	14.4 mg/dL	246 µmol/L	Isoniazid	6 mg/dL	438 µmol/L
Amlodipine besylate	14 µg/dL	245 nmol/L	Kanamycin	9 mg/dL	186 µmol/L
Ammonium chloride	5.35 mg/dL	1 mmol/L	L-pipecolic acid	5.7 mg/dL	442 µmol/L
Amoxicillin	7.53 mg/dL	206 µmol/L	Levodopa	0.98 mg/dL	49.5 µmol/L
Amphotericin B	35.5 mg/dL	384 µmol/L	Levothyroxine	100 µg/dL	1.29 µmol/L
Ascorbic acid	60 mg/dL	3.42 mmol/L	Lidocaine	1.5 mg/dL	64 µmol/L
Atorvastatin calcium	69.3 mg/dL	600 µEq/L	Lithium Acetoacetate	324 mg/dL	30 mmol/L
Benazepril	2.04 mg/dL	48 µmol/L	Lovastatin	21 µg/dL	0.519 µmol/L
β-hydroxybutyrate	157 mg/dL	12.46 mmol/L	Metformin	4.0 mg/dL	310 µmol/L
Bilirubin, conjugated	57.65 mg/dL	684 µmol/L	Metronidazole	12.3 mg/dL	719 µmol/L
Bilirubin, unconjugated	40 mg/dL	684 µmol/L	N-Acetylcysteine	166.5 mg/dL	10.2 mmol/L
Calcium dobesilate	6 mg/dL	144 µmol/L	Nafcillin	11.1 mg/dL	268 µmol/L
Carbenicillin	1.43 mg/dL	37.8 µmol/L	Naproxen	50 mg/dL	2170 µmol/L
Cefazolin	120 mg/dL	2643 µmol/L	N-Ethyl glycine	0.53 mg/dL	51.2 µmol/L
Cefoxitin	663 mg/dL	15.5 mmol/L	Nitrofurantoin	0.4 mg/dL	16.8 µmol/L
Ceftriaxone	81 mg/dL	1460 µmol/L	Omeprazole	0.84 mg/dL	24.3 µmol/L

Compound	Concentration		Compound	Concentration	
Cefuroxime	60.1 mg/dL	1416 µmol/L	Oxycodone	0.05 mg/dL	1.59 µmol/L
Cephalothin	180 mg/dL	4540 µmol/L	pH	6.8	6.8
Cholesterol	500 mg/dL	13 mmol/L	pH	8.8	8.8
Clindamycin (Cleocin)	5.1 mg/dL	120 µmol/L	Phenobarbital	69 mg/dL	2970 µmol/L
Cloxacillin	4.5 mg/dL	103.23 µmol/L	Polymyxin B	3.61 mg/dL	30 µmol/L
Creatine	9 mg/dL	707 mmol/L	Polymyxin E (Colistin)	2.7 mg/dL	23.1 µmol/L
Cyclosporin-a	0.563 mg/dL	4.69 µmol/L	Proline	24 mg/dL	2.085 mmol/L
Dextran 40	6 g/dL	60 g/L	Propranolol	0.2 mg/dL	7.71 µmol/L
Diphenhydramine	0.50 mg/dL	19.6 µmol/L	Pseudoephedrine	1 mg/dL	60.5 µmol/L
Dipyrone (Metamizole)	18 mg/dL	540 µmol/L	Pyruvate	17.6 mg/dL	2 mmol/L
Dobutamine	121 µg/dL	4.01 µmol/L	Rifampicin (Rifampin)	6.43 mg/dL	78.1 µmol/L
Dopamine	90 µg/dL	5.87 µmol/L	Salicylic acid	60 mg/dL	4.34 µmol/L
Doxycycline	3.0 mg/dL	67.5 µmol/L	Sodium bicarbonate	336 mg/dL	40 mmol/L
Entecavir	2.3 µg/dL	0.083 µmol/L	Spironolactone	0.06 mg/dL	1.44 µmol/L
Ethambutol	3 mg/dL	147 µmol/L	Streptomycin	12.9 mg/dL	444 µmol/L
Ethamsylate	6 mg/dL	228 µmol/L	Sulbactam	3 mg/dL	128.7 µmol/L
Ethanol	599 mg/dL	130 mmol/L	Sulfamethoxazole	40 mg/dL	1.58 mmol/L
Flucytosine	30 mg/dL	2.33 mmol/L	Sulfapyridine	30 mg/dL	1200 µmol/L
Furosemide	6 mg/dL	181 µmol/L	Sulfasalazine	30 mg/dL	754 µmol/L
Gadodiamide	86.0 mg/dL	1.5 mmol/L	Tenofovir disoproxil	177 µg/dL	3.41 µmol/L
Gentamicin	3 mg/dL	62.8 µmol/L	Tetracycline	2.4 mg/dL	54 µmol/L
Gentisic acid	1.8 mg/dL	117 µmol/L	Theophylline	6 mg/dL	333 µmol/L
Glipizide	0.30 mg/dL	6.73 µmol/L	Tolazamide	40 mg/dL	1284 µmol/L
Glucose	1000 mg/dL	56 mmol/L	Tolbutamide	64.1 mg/dL	2.37 mmol/L
Glutathione	92 mg/dL	3 mmol/L	Triglycerides	1500 mg/dL	16.9 mmol/L
Glyburide (Glybenclamide)	0.192 mg/dL	3.89 µmol/L	Trimethoprim	4.2 mg/dL	145 µmol/L
Glycine ethyl ester	0.71 mg/dL	51.2 µmol/L	Uric acid	23.5 mg/dL	1400 mmol/L
Glycocyamidine	4.4 mg/dL	442 µmol/L	Vancomycin	12 mg/dL	82.8 µmol/L
Hemoglobin	1000 mg/dL	155 µmol/L	Warfarin	7.5 mg/dL	243 µmol/L

Urine

The substances listed in the table below were tested with the UREA test within VITROS UREA-CREA Slides following CLSI EP07[13,14] and found not to interfere, bias < 90 mg/dL (< 32 mmol/L) at 900 mg/dL (321 mmol/L) urea N and bias < 140 mg/dL (< 50 mmol/L) at 1400 mg/dL (500 mmol/L) urea N at the concentration shown.

Compound	Concentration	
10% Thymol in isopropanol*	3.3 mL/L	3.3 mL/L
Ammonium chloride	5.35 mg/dL	1 mmol/L
Ascorbic acid	201 mg/dL	11.4 mmol/L
Bilirubin, conjugated	57.65 mg/dL	684 µmol/L
Bilirubin, unconjugated	40 mg/dL	684 µmol/L
Creatine	131.1 mg/dL	10 mmol/L
Hemoglobin	1000 mg/dL	155 µmol/L
Intralipid	800 mg/dL	8 g/L
Lithium Acetoacetate	324 mg/dL	30 mmol/L
Magnesium chloride	571 mg/dL	60 mmol/L
Pyruvate	17.6 mg/dL	2 mmol/L
Rifampicin (Rifampin)	4.5 mg/dL	54.7 µmol/L
Sodium bicarbonate	672 mg/dL	80 mmol/L
Sodium fluoride*	5 g/L	119 mmol/L
Sodium formate*	3.35 mg/dL	49.3 mmol/L
Sodium oxalate	60 mg/dL	4.5 mmol/L
Toluene*	1.3 mL/L	12.3 mmol/L
Total Protein	50 mg/dL	0.5 g/L
Uric acid	23.5 mg/dL	1400 µmol/L

* Substance is a common urine preservative

INSTRUCTIONS FOR USE

CREA

CREA Test

Creatinine

Rx ONLY

Intended Use

For *in vitro* diagnostic use only.

The CREA test within the VITROS XT Chemistry Products UREA-CREA Slides quantitatively measures creatinine (CREA) concentration in serum, plasma, and urine using VITROS XT 7600 Integrated Systems. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

Summary and Explanation of the Test

Serum creatinine and urinary creatinine excretion is a function of lean body mass in normal persons and shows little or no response to dietary changes. The serum creatinine concentration is higher in men than in women. Since urinary creatinine is excreted mainly by glomerular filtration, with only small amounts due to tubular secretion, serum creatinine and a 24-hour urine creatinine excretion can be used to estimate the glomerular filtration rate.

Serum creatinine is increased in acute or chronic renal failure, urinary tract obstruction, reduced renal blood flow, shock, dehydration, and rhabdomyolysis. Causes of low serum creatinine concentration include debilitation and decreased muscle mass. Exercise may cause an increased creatinine clearance. The creatinine clearance rate is unreliable if the urine flow is low.

Principles of the Procedure

The CREA test is a multilayered, analytical element coated on a polyester support.

A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers. Creatinine diffuses to the reagent layer, where it is hydrolyzed to creatine in the rate-determining step. The creatine is converted to sarcosine and urea by creatine amidinohydrolase. The sarcosine, in the presence of sarcosine oxidase, is oxidized to glycine, formaldehyde, and hydrogen peroxide. The final reaction involves the peroxidase-catalyzed oxidation of a leuco dye to produce a colored product.

Following addition of the sample, the slide is incubated. During the initial reaction phase, endogenous creatine in the sample is oxidized. The resulting change in reflection density is measured at 2 time points.

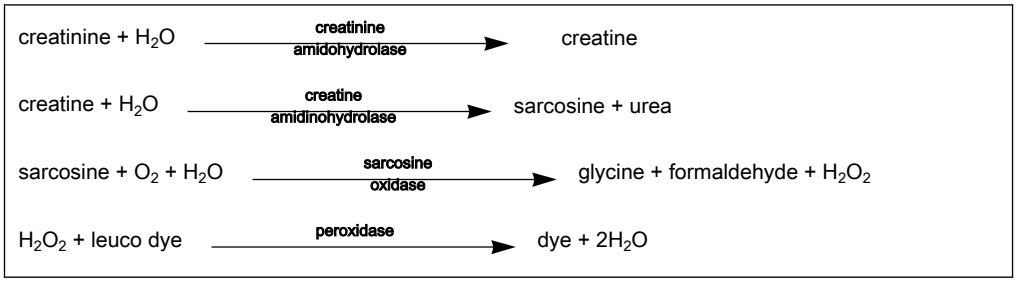
The difference in reflection density is proportional to the concentration of creatinine present in the sample.

Test Type and Conditions

Test Type	VITROS System*	Approximate Incubation Time	Temperature	Wavelength	Reaction Sample Volume
Two-point rate	XT 7600	5.0 minutes	37 °C (98.6 °F)	670 nm	3.2 µL

* Not all products and systems are available in all countries.

Reaction Scheme



Warnings and Precautions

For *in vitro* diagnostic use only.

WARNING:	Take care when handling materials and samples of human origin. Since no test method can offer complete assurance that infectious agents are absent, consider all clinical specimens, controls, and calibrators potentially infectious. Handle specimens, solid and liquid waste, and test components in accordance with local regulations and CLSI Guideline M29[2] or other published biohazard safety guidelines.

For specific warnings and precautions for calibrators, quality control materials, and other components, refer to the Instructions for Use for the appropriate VITROS product, or to other manufacturer's product literature.

Reagents

Slide Ingredients

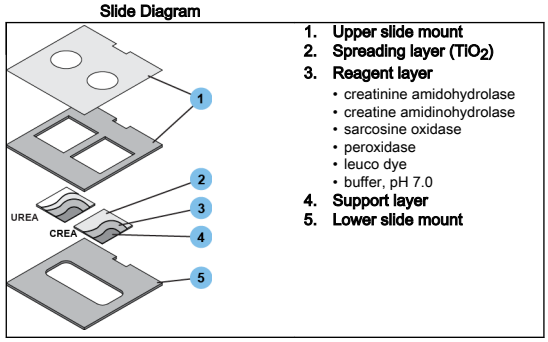
Reactive Ingredients per cm²

Creatinine amidohydrolase (*Flavobacterium sp.,*) 0.20 U; creatine amidinohydrolase (*Alcaligenes sp.,*) 3.6 U; sarcosine oxidase (*Bacillus sp.*) 0.55 U; peroxidase (horseradish root) 1.6 U and 2-(3,5-dimethoxy-4-hydroxyphenyl)-4,5-bis(4-dimethylaminophenyl) imidazole (leuco dye) 32 µg.

Other Ingredients

Pigment, binders, surfactants, stabilizer, scavenger, chelator, buffer, dye solubilizer and cross-linking agent.

Slide Diagram



1. **Upper slide mount**
2. **Spreading layer (TiO_2)**
3. **Reagent layer**
   - creatinine amidohydrolase
   - creatine amidinohydrolase
   - sarcosine oxidase
   - peroxidase
   - leuco dye
   - buffer, pH 7.0
4. **Support layer**
5. **Lower slide mount**

Reagent Handling

Caution:	Do not use slide cartridges with damaged or incompletely sealed packaging.

- Inspect the packaging for signs of damage.
- Be careful when opening the outer packaging with a sharp instrument so as to avoid damage to the individual product packaging.

Reagent Preparation

IMPORTANT:	The slide cartridge must reach room temperature, 18–28 °C (64–82 °F), before it is unwrapped and loaded into the slide supply.

1. Remove the slide cartridges from storage.
2. Warm the wrapped cartridge at room temperature for 30 minutes when taken from the refrigerator or 60 minutes from the freezer.
3. Unwrap and load the cartridge into the slide supply.

Note:	Load the cartridges within 24 hours after they reach room temperature, 18–28 °C (64–82 °F).

Reagent Storage and Stability

VITROS XT UREA-CREA Slides are stable until the expiration date on the carton when they are stored and handled as specified. Do not use beyond the expiration date.

Reagent	Storage Condition		Stability
Unopened	Refrigerated	2–8 °C (36–46 °F)	≤ 4 weeks
	Frozen	≤ -18 °C (≤ 0 °F)	Until expiration date
Opened	On-analyzer	System turned on	≤ 2 weeks
	On-analyzer	System turned off	≤ 2 hours

- Do not store with or near ammonia, ammonia compounds, or amines.
- Verify performance with quality control materials:
  - If the system is turned off for more than 2 hours.
  - After reloading cartridges that have been removed from the slide supply and stored for later use.

Specimen Collection, Preparation and Storage

Specimens Recommended

- Serum
- Plasma: Heparin (lithium and sodium)
- Urine

IMPORTANT: Certain collection devices have been reported to affect other analytes and tests.[3] Owing to the variety of specimen collection devices available, Ortho Clinical Diagnostics is unable to provide a definitive statement on the performance of its products with these devices. Confirm that your collection devices are compatible with this test.

Specimens Not Recommended

Do not use specimens obtained through catheters used to infuse hyperalimentation fluid. Refer to “Limitations of the Procedure.”

Serum and Plasma

Specimen Collection and Preparation

Collect specimens using standard laboratory procedures.[5,6]

Note: For details on minimum fill volume requirements, refer to the operating instructions for your system.

Patient Preparation

No special patient preparation is necessary.

Special Precautions

Centrifuge specimens and remove the serum or plasma from the cellular material within 4 hours of collection.[4]

Specimen Handling and Storage

- Handle and store specimens in stoppered containers to avoid contamination and evaporation.
- Mix samples by gentle inversion and bring to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Specimen Storage and Stability: Serum and Plasma

Storage	Temperature	Stability
Room temperature	18–28 °C (64–82 °F)	≤ 5 days
Refrigerated	2–8 °C (36–46 °F)	≤ 30 days
Frozen	≤ -18 °C (≤ 0 °F)	≤ 6 months

Urine

Specimen Collection and Preparation

- Collect specimens using standard laboratory procedures.[7]
- Keep refrigerated until analysis.

Note: For details on minimum fill volume requirements, refer to the operating instructions for your system.

Patient Preparation

No special patient preparation is necessary.

Special Precautions

Urine specimens must be pretreated prior to processing. Refer to “Specimen Pretreatment” for instructions.

Specimen Handling and Storage

- Handle and store specimens in stoppered containers to avoid contamination and evaporation.
- Mix samples by gentle inversion and bring to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Specimen Storage and Stability: Urine

Storage	Temperature	Stability
Room temperature	18–28 °C (64–82 °F)	≤ 3 days
Refrigerated	2–8 °C (36–46 °F)	≤ 5 days
Frozen	≤ -18 °C (≤ 0 °F)	≤ 6 months

Specimen Pretreatment

Urine

Predilution

Pretreatment is managed by the analyzer, no operator intervention is required.

Testing Procedure

Materials Provided

VITROS XT Chemistry Products UREA-CREA Slides

Materials Required but Not Provided

- VITROS Chemistry Products Calibrator Kit 1
- Quality control materials, such as VITROS Chemistry Products Performance Verifier I and II for serum and plasma
- VITROS Chemistry Products 7% BSA
- Reagent-grade water
- VITROS Chemistry Products FS Diluent Pack 2 (BSA/Saline) (for on-analyzer dilution of serum and plasma samples)
- VITROS Chemistry Products FS Diluent Pack 3 (Specialty Diluent/Water) (for on-analyzer dilution of urine samples)

Operating Instructions

- Check reagent inventories at least daily to ensure that quantities are sufficient for the planned workload.
- For additional information, refer to the operating instructions for your system.

IMPORTANT:	Bring all fluids and samples to room temperature, 18–28 °C (64–82 °F), prior to analysis.

Sample Dilution

Serum and Plasma

If creatinine concentrations exceed the system's measuring (reportable or dynamic) range or if the analyzer displays a DP code (indicating high background density, usually due to an elevated creatine concentration):

On-Analyzer Sample Dilution

Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure.
For VITROS XT 7600 Integrated Systems, use VITROS Chemistry Products FS Diluent Pack 2 for the dilution.

Manual Sample Dilution

1. Dilute the sample with 1 part sample and 1 part VITROS 7% BSA.
2. Reanalyze.
3. Multiply the results by 2 to obtain an estimate of the original sample's creatinine concentration.

Urine

If creatinine concentrations exceed the system's measuring (reportable or dynamic) range:

On-Analyzer Sample Dilution

Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure.
For VITROS XT 7600 Integrated Systems, use VITROS Chemistry Products FS Diluent Pack 3 for the dilution.

Manual Sample Dilution

1. Dilute the sample with 1 part sample and 1 part reagent-grade water.
2. Reanalyze.
3. Multiply the results by 2 to obtain an estimate of the original sample's creatinine concentration.

Calibration

Required Calibrators

VITROS Chemistry Products Calibrator Kit 1

Note: The same VITROS Calibrator Kit is used to calibrate serum, plasma, and urine creatinine. However, specific supplementary assigned values (SAVs) are applied for each body fluid.

Calibrator Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Calibrator Kit 1.

Calibration Procedure

Refer to the operating instructions for your system.

When to Calibrate

Calibrate:

- When the slide lot number changes.
- When critical system parts are replaced due to service or maintenance.
- When government regulations require.
  For example, in the USA, CLIA regulations require calibration or calibration verification at least once every six months.

The CREA test within the VITROS XT UREA-CREA Slides may also need to be calibrated:

- If quality control results are consistently outside acceptable range.
- After certain service procedures have been performed.

For additional information, refer to the operating instructions for your system.

Calculations

Reflectance from the slide is read at 670 nm at two fixed time points during the incubation period, and the change in reflectance between these two readings is calculated. Once a calibration has been performed for each slide lot, creatinine concentration in unknown samples can be determined using the software-resident two-point rate math model and the change in reflectance calculated for each unknown test slide.

Validity of a Calibration

Calibration parameters are automatically assessed by the system against a set of quality parameters detailed in Review Assay Data screen on VITROS XT Integrated Systems. Failure to meet any of the pre-defined quality parameters results in a failed calibration. The calibration report should be used in conjunction with quality control results to determine the validity of a calibration.

Measuring (Reportable or Dynamic) Range

Fluid	Conventional Units (mg/dL)	SI Units (µmol/L)	Alternate Units (mg/L)
Serum/Plasma	0.15–14.0	13–1238	1.5–140
Urine*	3.2–346.5	283–30631	32–3465

* After multiplying by a dilution factor of 21.

For out-of-range samples, refer to “Sample Dilution.”

Traceability of Calibration

The values assigned to the VITROS Chemistry Products Calibrator Kit 1 for Creatinine are traceable to a Gas Chromatography Isotope Dilution Mass Spectrometry (GC/IDMS) method[21] and National Institute of Standards and Technology (NIST) SRM® 914 creatinine standard reference material.

Quality Control

Quality Control Material Selection

IMPORTANT: VITROS Performance Verifiers are recommended for use with VITROS XT Integrated Systems. Evaluate the performance of other commercial control fluids for compatibility with this test before using for quality control.

- Controls that are reconstituted with deionized water should perform acceptably.
- Control materials other than VITROS Performance Verifiers may show a difference when compared with other creatinine methods if they:
  - Depart from a true human matrix.
  - Contain high concentrations of preservatives, stabilizers, or other nonphysiological additives.
- Liquid serum and urine controls often contain high creatine levels and may give DP codes.
- Do not use control materials stabilized with ethylene glycol.

Urine

For urine specimens, use commercially available urine control materials.

IMPORTANT: If using a VITROS XT Integrated Systems in On-Analyzer Dilution Mode, do not manually dilute samples for analysis and do not multiply by a dilution factor after analysis. Refer to the operating instructions for your system for more information on the On-Analyzer Dilution Procedure.

Quality Control Procedure Recommendations

- Choose control levels that check the clinically relevant range.
- Analyze quality control materials in the same manner as patient samples, before or during patient sample processing.
- To verify system performance, analyze control materials:
  - After calibration.
  - According to local regulations or at least once each day that the test is being performed.
  - After specified service procedures are performed. Refer to the operating instructions for your system.
- If control results fall outside your acceptable range, investigate the cause before deciding whether to report patient results.
- For general quality control recommendations, refer to *Statistical Quality Control for Quantitative Measurements: Principles and Definitions; Approved Guideline-Fourth Edition* [11] or other published guidelines.
- For additional information, refer to the operating instructions for your system.

Quality Control Material Preparation, Handling, and Storage

Refer to the Instructions for Use for VITROS Chemistry Products Performance Verifier I and II or to other manufacturer's product literature.

Results

Reporting Units and Unit Conversion

The VITROS XT Systems may be programmed to report CREA results in conventional, SI, and alternate units.

Conventional Units	SI Units	Alternate Units
mg/dL	µmol/L (mg/dL x 88.4)	mg/L (mg/dL x 10)

Limitations of the Procedure

Known Interferences

Serum and Plasma

- **Creatine**: At a creatinine concentration of 1.5 mg/dL (133 µmol/L), creatine greater than 8 mg/dL (707 µmol/L) will be flagged with a DP code (because highly elevated creatine concentrations may cause excessive background density). For unflagged samples, residual bias because of creatine will be less than 0.15 mg/dL (13 µmol/L). At a creatinine concentration of 14 mg/dL (1237 µmol/L), creatine greater than 1 mg/dL (88 µmol/L) will be flagged with a DP code. Residual bias for unflagged samples will be less than 2%. Refer to “Sample Dilution” for dilution instructions.
- **Proline**: Patients receiving hyperalimentation fluids containing proline may show an increase of 0.2 mg/dL (18 µmol/L). Do not collect specimens from intravenous fluid lines contaminated with hyperalimentation fluid.

The VITROS XT Chemistry Products UREA-CREA Slides method was screened for interfering substances following CLSI EP07.[13,14] The substances listed in the table, when tested at the concentrations indicated, caused the bias shown.

For substances that were tested and did not interfere, refer to “Specificity.”

Interferent*	Interferent Concentration		Creatinine Concentration		Bias**	
	Conv. Units	SI Units	Conv. Units (mg/dL)	SI Units (µmol/L)	Conv. Units (mg/dL)	SI Units (µmol/L)
Bilirubin, conjugated	58 mg/dL	684 µmol/L	1.6	140	-0.16	-14
Dipyrone (Metamizole)***	9 mg/dL	270 µmol/L	1.6	144	-0.20	-18
	14 mg/dL	405 µmol/L	4.9	434	-0.73	-64
Ethamsylate	4.1 mg/dL	156 µmol/L	1.7	152	-0.18	-16
Glutathione	69 mg/dL	2.25 mmol/L	1.6	144	-0.23	-20
N-Ethyl glycine****	0.40 mg/dL	38 mmol/L	1.7	147	0.21	18
Proline	18 mg/dL	1564 µmol/L	1.7	152	0.24	21
Tolazamide	5.0 mg/dL	161 µmol/L	1.6	138	-0.24	-21
			4.6	409	-0.55	-49
Total protein	15 g/dL	150 g/L	1.7	151	0.26	23
	12 g/dL	120 g/L	5.0	439	0.53	47

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

** The bias is an estimate of the maximum bias observed.

*** Dipyrone at 9 mg/dL is equivalent to 6X the equivalent of a 1000 mg oral dose, or 1.5X the equivalent of a 1000 mg intravenous dose.[22]

**** N-ethyl glycine is a metabolite of lidocaine and may be present at high levels in patients on long-term lidocaine therapy.[23]

Other Limitations

Certain drugs and clinical conditions are known to alter creatinine concentration *in vivo*. For additional information, refer to one of the published summaries.[15,16]

Expected Values

IMPORTANT: If using results to calculate an estimated glomerular filtration rate (eGFR), confirm that you are using the appropriate MDRD (Modification of Diet in Renal Disease) equation.[24]

Reference Interval

The serum reference intervals are the central 95% of results from an external study of apparently healthy adults (serum: 180 males and 180 females).

The urine reference intervals are based on a separate external study.[25]

	Conventional Units	SI Units	Alternate Units
Serum			
Male	0.66–1.25 mg/dL	58–110 µmol/L	6.6–12.5 mg/L
Female	0.52–1.04 mg/dL	46–92 µmol/L	5.2–10.4 mg/L
Urine			
Male	1000–2000 mg/day*	8840–17680 µmol/day**	1000–2000 mg/day***
Female	800–1800 mg/day*	7072–15912 µmol/day**	800–1800 mg/day***

* Creatinine concentration (mg/dL) x 24-hour volume (dL) = mg/day.

** Creatinine concentration (µmol/L) x 24-hour volume (L) = µmol/day.

*** Creatinine concentration (mg/L) x 24-hour volume (L) = mg/day.

Each laboratory should confirm the validity of these intervals for the population it serves.

Performance Characteristics

Detection Capability

The Limit of Quantitation (LoQ) for the CREA test within the VITROS XT UREA-CREA Slides is 0.15 mg/dL for serum/plasma and 3.2 mg/dL for urine. The total number of LoQ determinations was 72 for serum and 64 for urine. The LoQ was established consistent with CLSI EP17.[18]

Fluid Type	LoQ*	
	Conventional Units mg/dL	SI Units µmol/L
Serum/Plasma	0.15	13
Urine	3.2	283

* The Total Error goal used to accept the LoQ was ≤ 0.06 mg/dL for serum and ≤ 1.2 mg/dL for urine.

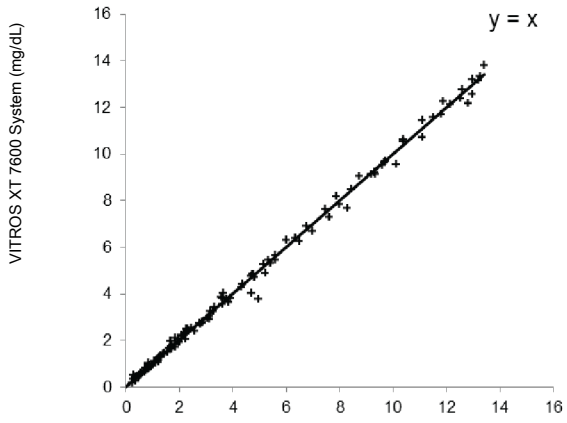
Method Comparison

The plots and tables below show the results of a method comparison study with serum samples and urine samples analyzed on the VITROS XT 7600 Integrated System and with the Ortho Clinical Diagnostics comparative method (an HPLC method),[26] which has demonstrated equivalence to the Gas Chromatography Isotope Dilution Mass Spectrometry (GC/IDMS) reference method.

The tables also show the results of comparisons with serum and urine samples between the VITROS XT 7600 Integrated System and the VITROS Chemistry Products CREA Slides on a VITROS 5600 Integrated System. Testing followed CLSI EP09.[19]

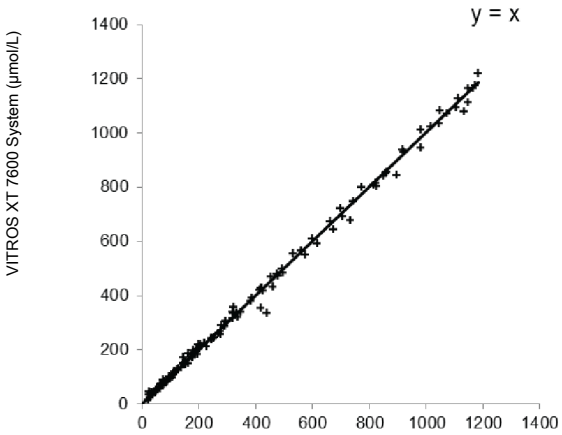
Serum

Conventional Units



Comparative Method: HPLC (mg/dL)

SI Units

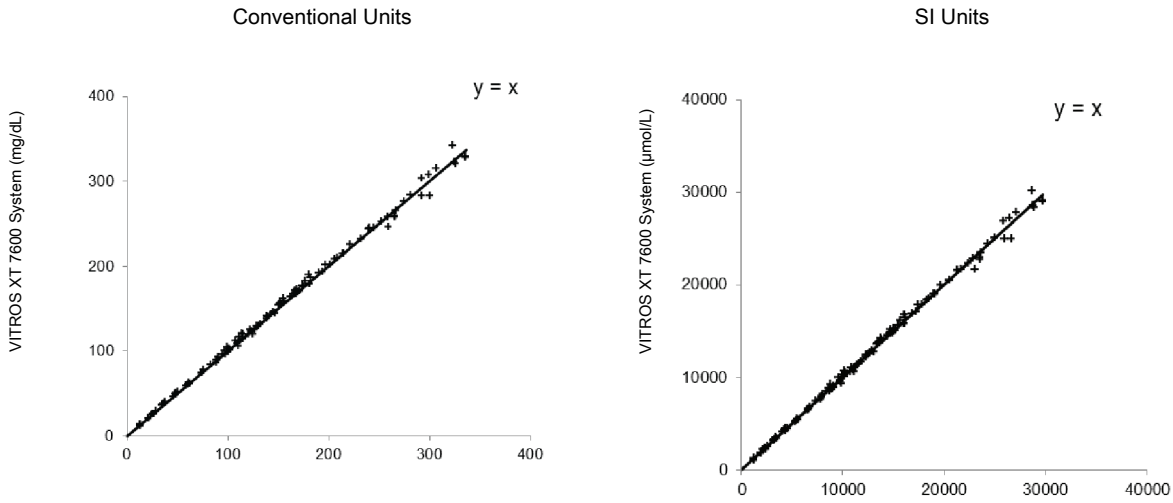


Comparative Method: HPLC (µmol/L)

				Conventional Units (mg/dL)			SI Units (µmol/L)		
	n	Slope	Correlation Coefficient	Range of Sample Conc.	Intercept	Sy.x	Range of Sample Conc.	Intercept	Sy.x
XT 7600 vs. Comparative Method	130	1.01	0.999	0.26–13.40	-0.01	0.21	23–1185	-0.48	18.54
XT 7600 vs. 5600†	130	1.00	1.000	0.20 –13.49	-0.01	0.09	17–1193	-0.65	8.16

† Comparisons made using the same patient samples tested with the VITROS Chemistry Products CREA Slides run on the VITROS 5600 Integrated System.

Urine



				Conventional Units (mg/dL)			SI Units (µmol/L)		
	n	Slope	Correlation Coefficient	Range of Sample Conc.	Intercept	Sy.x	Range of Sample Conc.	Intercept	Sy.x
XT 7600 vs. Comparative Method	116	1.01	0.999	13.6–336.6	-0.83	4.30	1207–29758	-73.45	380.12
XT 7600 vs. 5600†	116	1.01	0.998	13.0–336.6	-0.93	5.36	1151–29751	-82.54	474.18

† Comparisons made using the same patient samples tested with the VITROS Chemistry Products CREA Slides run on the VITROS 5600 Integrated System.

Precision

Precision was evaluated with patient pools and quality control materials on the VITROS XT 7600 Integrated System following CLSI EP05.[20] The data presented are a representation of test performance and are provided as a guideline. Variables such as sample handling and storage, reagent handling and storage, laboratory environment and system maintenance can affect reproducibility of test results.

Serum

System	Conventional Units (mg/dL)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	0.66	0.007	1.1	0.008	1.2	0.011	1.7	80	20
	0.85	0.010	1.2	0.012	1.4	0.014	1.6	80	20
	0.86	0.012	1.4	0.012	1.4	0.014	1.6	80	20
	5.41	0.030	0.6	0.040	0.7	0.084	1.6	80	20
	9.41	0.068	0.7	0.072	0.8	0.163	1.7	80	20
	12.62	0.090	0.7	0.107	0.8	0.220	1.7	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

System	SI Units (µmol/L)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	58	0.6	1.0	0.7	1.1	1.0	1.6	80	20
	75	0.9	1.2	1.0	1.3	1.3	1.7	80	20
	76	1.1	1.4	1.1	1.4	1.2	1.6	80	20
	478	2.6	0.5	3.5	0.7	7.4	1.6	80	20
	831	6.0	0.7	6.4	0.8	14.4	1.7	80	20
	1116	7.9	0.7	9.4	0.8	19.4	1.7	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

Urine

System	Conventional Units (mg/dL)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	39.0	0.26	0.7	0.37	1.0	0.52	1.3	80	20
	58.5	0.67	1.1	0.90	1.5	1.14	2.0	80	20
	137.5	1.47	1.1	2.20	1.6	3.15	2.3	80	20
	239.4	2.13	0.9	2.27	0.9	3.13	1.3	80	20
	317.2	2.00	0.6	4.13	1.3	5.44	1.7	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

System	SI Units (µmol/L)							No. of Obs.	No. of Days
	Mean Concentration	Repeatability*		Within Day**		Within Lab***			
		SD	CV %	SD	CV %	SD	CV %		
XT 7600	3446	23	0.7	33	1.0	46	1.3	80	20
	5169	59	1.1	79	1.5	101	2.0	80	20
	12156	130	1.1	194	1.6	279	2.3	80	20
	21161	188	0.9	200	0.9	277	1.3	80	20
	28042	176	0.6	365	1.3	481	1.7	80	20

* Repeatability (formerly called within-run precision) was determined using two replicates per run.

** Within Day precision was determined using two runs per day with two replications per run.

*** Within Lab precision was determined using a single lot of slides and a single calibration.

Specificity

Substances that Do Not Interfere

Serum and Plasma

The substances listed in the table below were tested with the CREA test within VITROS XT UREA-CREA Slides following CLSI EP07[13,14] and found not to interfere, bias < 0.13 mg/dL (< 11.8 µmol/L) at 1.5 mg/dL (132.6 µmol/L) and bias < 0.44 mg/dL (< 39.2 µmol/L) at 5 mg/dL (442.0 µmol/L), at the concentration shown.

Compound	Concentration		Compound	Concentration	
5-Aminosalicylic acid	2.04 mg/dL	133 µmol/L	Ibuprofen	50 mg/dL	2425 µmol/L
6-mercaptopurine	0.2 mg/dL	13.1 µmol/L	Insulin	3.12 µg/dL	5.38 nmol/L
Acetaminophen	20 mg/dL	1324 µmol/L	Intralipid	2000 mg/dL	20 g/L
Alprazolam	0.2 mg/dL	6.48 µmol/L	Isoniazid	6 mg/dL	438 µmol/L
Amikacin	14.4 mg/dL	246 µmol/L	Kanamycin	9 mg/dL	186 µmol/L
Amlodipine besylate	14 µg/dL	245 nmol/L	L-pipecolic acid	5.7 mg/dL	442 µmol/L
Ammonium chloride	5.35 mg/dL	1 mmol/L	Levodopa	0.98 mg/dL	49.5 µmol/L
Amoxicillin	7.53 mg/dL	206 µmol/L	Levothyroxine	100 µg/dL	1.29 µmol/L
Amphotericin B	35.5 mg/dL	384 µmol/L	Lidocaine	1.5 mg/dL	64 µmol/L

Compound	Concentration		Compound	Concentration	
Ascorbic acid	60 mg/dL	3.42 mmol/L	Lithium Acetoacetate	324 mg/dL	30 mmol/L
Atorvastatin calcium	69.3 mg/dL	600 µEq/L	Lovastatin	21 µg/dL	0.519 µmol/L
Benazepril	2.04 mg/dL	48 µmol/L	Metformin	4.0 mg/dL	310 µmol/L
β-hydroxybutyrate	157 mg/dL	12.46 mmol/L	Metronidazole	12.3 mg/dL	719 µmol/L
Bilirubin, unconjugated	40 mg/dL	684 µmol/L	N-Acetylcysteine	15 mg/dL	0.92 mmol/L
Calcium dobesilate	6 mg/dL	144 µmol/L	Nafcillin	11.1 mg/dL	268 µmol/L
Carbenicillin	1.43 mg/dL	37.8 µmol/L	Naproxen	50 mg/dL	2170 µmol/L
Cefazolin	120 mg/dL	2643 µmol/L	Nitrofurantoin	0.4 mg/dL	16.8 µmol/L
Cefoxitin	663 mg/dL	15.5 mmol/L	Omeprazole	0.84 mg/dL	24.3 µmol/L
Ceftriaxone	81 mg/dL	1460 µmol/L	Oxycodone	0.05 mg/dL	1.59 µmol/L
Cefuroxime	60.1 mg/dL	1416 µmol/L	pH	6.8	6.8
Cephalothin	180 mg/dL	4540 µmol/L	pH	8.8	8.8
Cholesterol	500 mg/dL	13 mmol/L	Phenobarbital	69 mg/dL	2970 µmol/L
Clindamycin (Cleocin)	5.1 mg/dL	120 µmol/L	Polymyxin B	3.61 mg/dL	30 µmol/L
Cloxacillin	4.5 mg/dL	103.23 µmol/L	Polymyxin E (Colistin)	2.7 mg/dL	23.1 µmol/L
Cyclosporin-a	0.563 mg/dL	4.69 µmol/L	Propranolol	0.2 mg/dL	7.71 µmol/L
Dextran 40	6 g/dL	60 g/L	Pseudoephedrine	1 mg/dL	60.5 µmol/L
Diphenhydramine	0.50 mg/dL	19.6 µmol/L	Pyruvate	17.6 mg/dL	2 mmol/L
Dobutamine	121 µg/dL	4.01 µmol/L	Rifampicin (Rifampin)	4.8 mg/dL	58.6 µmol/L
Dopamine	90 µg/dL	5.87 µmol/L	Salicylic acid	60 mg/dL	4.34 µmol/L
Doxycycline	3.0 mg/dL	67.5 µmol/L	Sodium bicarbonate	336 mg/dL	40 mmol/L
Entecavir	2.3 µg/dL	0.083 µmol/L	Spironolactone	0.06 mg/dL	1.44 µmol/L
Ethambutol	3 mg/dL	147 µmol/L	Streptomycin	12.9 mg/dL	444 µmol/L
Ethanol	599 mg/dL	130 mmol/L	Sulbactam	3 mg/dL	128.7 µmol/L
Flucytosine	30 mg/dL	2.33 mmol/L	Sulfamethoxazole	40 mg/dL	1.58 mmol/L
Furosemide	6 mg/dL	181 µmol/L	Sulfapyridine	30 mg/dL	1200 µmol/L
Gadodiamide	86.0 mg/dL	1.5 mmol/L	Sulfasalazine	30 mg/dL	754 µmol/L
Gentamicin	3 mg/dL	62.8 µmol/L	Tenofovir disoproxil	177 µg/dL	3.41 µmol/L
Gentisic acid	1.8 mg/dL	117 µmol/L	Tetracycline	2.4 mg/dL	54 µmol/L
Glipizide	0.30 mg/dL	6.73 µmol/L	Theophylline	6 mg/dL	333 µmol/L
Glucose	1000 mg/dL	56 mmol/L	Tolbutamide	64.1 mg/dL	2.37 mmol/L
Glyburide (Glybenclamide)	0.192 mg/dL	3.89 µmol/L	Triglycerides	1500 mg/dL	16.9 mmol/L
Glycine ethyl ester	0.71 mg/dL	51.2 µmol/L	Trimethoprim	4.2 mg/dL	145 µmol/L
Glycocyamidine	4.4 mg/dL	442 µmol/L	Uric acid	23.5 mg/dL	1400 mmol/L
Hemoglobin	1000 mg/dL	155 µmol/L	Vancomycin	12 mg/dL	82.8 µmol/L
Hypaque (diatrizoate)	19.28 mg/dL	314 µmol/L	Warfarin	7.5 mg/dL	243 µmol/L

Urine

The substances listed in the table below were tested with the CREA test within VITROS XT UREA-CREA Slides following CLSI EP07[13] ,[14] and found not to interfere, bias< 5.8 mg/dL (< 511 µmol/L) at 60 mg/dL (5304 µmol/L) and bias < 17 mg/dL (< 1503 µmol/L) at 200 mg/dL (17680 µmol/L) , at the concentration shown.

Compound	Concentration	
10% Thymol in isopropanol*	3.3 mL/L	3.3 mL/L
12N Hydrochloric acid*	6.7 mL/L	6.7 mL/L
Ammonium chloride	5.35 mg/dL	1 mmol/L
Ascorbic acid	201 mg/dL	11.4 mmol/L
Bilirubin, conjugated	57.65 mg/dL	684 µmol/L
Bilirubin, unconjugated	40 mg/dL	684 µmol/L
Boric acid*	5.3 mg/mL	85.7 mmol/L

Compound	Concentration	
Boric acid/Sodium formate (combined)*	5.3 mg/mL 3.35 mg/mL	85.7 mmol/L 49.3 mmol/L
Creatine	131.1 mg/dL	10 mmol/L
Glacial Acetic Acid*	10 mL/L	10 mL/L
Hemoglobin	1000 mg/dL	155 µmol/L
Intralipid	800 mg/dL	8 g/L
Lithium Acetoacetate	324 mg/dL	30 mmol/L
Magnesium chloride	571 mg/dL	60 mmol/L
Pyruvate	17.6 mg/dL	2 mmol/L
Rifampicin (Rifampin)	4.5 mg/dL	54.7 µmol/L
Sodium bicarbonate	672 mg/dL	80 mmol/L
Sodium fluoride*	5 g/L	119 mmol/L
Sodium formate*	3.35 mg/mL	49.3 mmol/L
Sodium oxalate	60 mg/dL	4.5 mmol/L
Toluene*	1.3 mL/L	12.3 mmol/L
Total Protein	50 mg/dL	0.5 g/L
Uric acid	23.5 mg/dL	1400 µmol/L

* Substance is a common urine preservative

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Glossary of Symbols

The following symbols may have been used in the labeling of this product.

Do Not Reuse	Upper Limit of Temperature	Range
Use by or Expiration Date (Year-Month-Day)	Lower Limit of Temperature	Range of Means
LOT Batch Code or Lot Number	Temperature Limitation	Midpoint
SN Serial Number	Consult Instructions for Use	Revised
REF Catalog Number or Product Code	Attention: The Instructions for Use (IFU) has been updated	Supersedes
Caution	S1 For use in Slide Supply 1	Contains Sufficient for "n" Tests
Manufacturer	S2 For use in Slide Supply 2	IVD *in vitro* Diagnostic Medical Device
Date of Manufacture	SI SI Units	Der Grüne Punkt (the Green Dot). Manufacturer follows certain packaging material waste disposal management regulations
EC REP Authorized Representative in the European Community	CONV Conventional Units	Estimated within-lab SD
	Value	
Corrosive	Flammable	Serious Health Hazards
Health Hazards	Acute Toxicity	Environmental or Aquatic Toxicity

Revision History

Date of Revision	Version	Description of Technical Changes*
2019-01-17	2.0	• Initial implementation in US • Updated (UREA-CREA): – Intended Use- Revised for clarity – Specimen Type- Added lithium and sodium – Sample Dilution- Manual Sample Dilution instructions updated for Serum/ Plasma and Urine – Limitations of the Procedure- Interferents Removed and Interferents Values updated in Serum/Plasma Table – Specificity- Bias Statement updated for Serum/Plasma and Urine, compounds added and concentration values updated in Serum/Plasma Table – References Removed • Updated (UREA): pH and Bias information removed from “Other Limitations”
2018-08-16	1.0	• Implemented for outside the US Only • Initial version of Instructions for Use

* The change bars indicate the position of a technical amendment to the text with respect to the previous version of the document.

When this Instructions For Use is replaced, sign and date below and retain as specified by local regulations or laboratory policies, as appropriate.

_____ _____

Signature Obsolete Date

CE

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