Piccolo® Kidney Check

For In Vitro Diagnostic Use and For Professional Use Only
Customer and Technical Service: 1-800-822-2947
Customers outside the US: +49 6155 780 210

Applicable to US customers only
CLIA Waived: Use lithium heparin whole blood, only
Moderate Complexity: Use lithium heparin whole blood, lithium heparin plasma, or serum

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1. Intended Use

The Piccolo® Kidney Check , used with the Piccolo Xpress chemistry analyzer, is intended to be used for the *in vitro* quantitative determination of creatinine and blood urea nitrogen (BUN) in heparinized whole blood, heparinized plasma, or serum in a clinical laboratory setting or point-of-care location.

For US Customers Only

The tests on this panel are waived under CLIA '88 regulations. If a laboratory modifies the test system instructions, then the tests are considered high complexity and subject to all CLIA requirements. For CLIA waived labs, only lithium heparin whole blood may be tested. For use in moderate complexity labs, lithium heparinized whole blood, lithium heparinized plasma, or serum may be used.

A CLIA Certificate of Waiver is needed to perform CLIA waived testing. A Certificate of Waiver can be obtained from the Centers for Medicare & Medicaid Services (CMS). Please contact the Commission on Laboratory Accreditation (COLA) at 1-800-981-9883 for assistance in obtaining one.

2. Summary and Explanation of Tests

The Piccolo Kidney Check reagent disc and the Piccolo Xpress chemistry analyzer comprise an *in vitro* diagnostic system that aids the physician in diagnosing the following disorders:

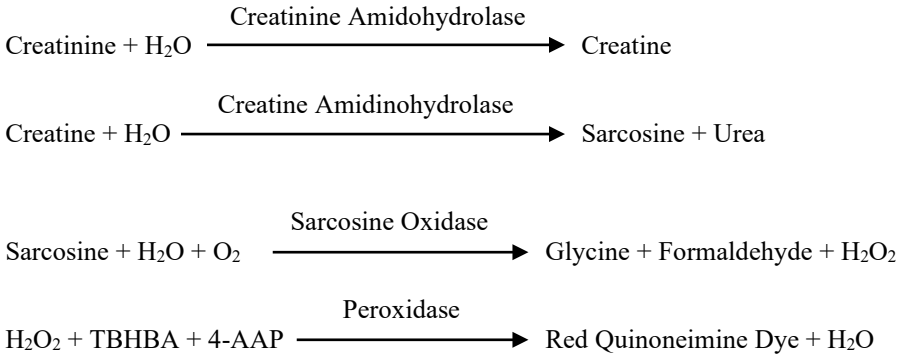
Creatinine:	Renal disease and monitoring of renal dialysis.
Blood urea nitrogen (BUN):	Renal and metabolic diseases.

As with any diagnostic test procedure, all other test procedures including the clinical status of the patient, should be considered prior to final diagnosis.

3. Test Principles

Creatinine (CRE)
The Jaffe method, first introduced in 1886, is still a commonly used method of determining creatinine levels in blood. The current reference method combines the use of fuller's earth (floridin) with the Jaffe technique to increase the specificity of the reaction.[1,2] Enzymatic methods have been developed that are more specific for creatinine than the various modifications of the Jaffe technique.[3,4,5] Methods using the enzyme creatinine amidohydrolase eliminate the problem of ammonium ion interference found in techniques using creatinine iminohydrolase.[6]

In the coupled enzyme reactions, creatinine amidohydrolase hydrolyzes creatinine to creatine. A second enzyme, creatine amidinohydrolase, catalyzes the formation of sarcosine from creatine. Sarcosine oxidase causes the oxidation of sarcosine to glycine, formaldehyde and hydrogen peroxide (H_2O_2). In a Trinder finish, peroxidase catalyzes the reaction among the hydrogen peroxide, 2,4,6-tribromo-3-hydroxybenzoic acid (TBHBA) and 4-aminoantipyrine (4-AAAP) into a red quinoneimine dye. Potassium ferrocyanide and ascorbate oxidase are added to the reaction mixture to minimize the potential interference of bilirubin and ascorbic acid, respectively.



Two cuvettes are used to determine the concentration of creatinine in the sample. Endogenous creatine is measured in the blank cuvette, which is subtracted from the combined endogenous creatine and the creatine formed from the enzyme reactions in the test cuvette. Once the endogenous creatine is eliminated from the calculations, the concentration of creatinine is proportional to the intensity of the red color produced. The endpoint reaction is measured as the difference in absorbance between 550 nm and 600 nm.

eGFR (calculated)

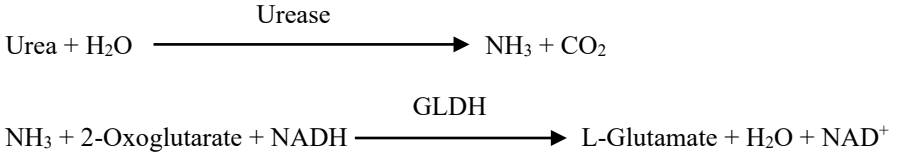
Serum creatinine is routinely measured as an indicator of renal function. Because creatinine is influenced by age, gender and race, chronic kidney disease (CKD) may not be detected using serum creatinine alone. Thus, the National Kidney Disease Education Program strongly recommends that laboratories routinely report an estimated Glomerular Filtration Rate (eGFR) when serum creatinine is measured for patients 18 and older. Routinely reporting the eGFR with all serum creatinine determinations allows laboratories to help identify individuals with reduced kidney function and help facilitate the detection of CKD. Calculated eGFR values of <60 ml/min are generally associated with increased risk of adverse outcomes of CKD.

Calculation of the eGFR is performed by the Piccolo using the patient's age, gender and race. The Piccolo method for creatinine is traceable to the IDMS reference method for creatinine so that the following form of the MDRD equation for calculating the eGFR can be used.

GFR (mL/min/1.73 m^2) = 175 x $(S_{cr})^{-1.154}$ x $(Age)^{-0.203}$ x (0.742 if female) x (1.212 if African American)

Blood Urea Nitrogen (BUN)
Urea can be measured both directly and indirectly. The diacetyl monoxime reaction, the only direct method to measure urea, is commonly used but employs dangerous reagents.[7] Indirect methods measure ammonia created from the urea; the use of the enzyme urease has increased the specificity of these tests.[8] The ammonia is quantitated by a variety of methods, including nesslerization (acid titration), the Berthelot technique[9,10] and coupled enzymatic reactions.[11,12] Catalyzed Berthelot procedures, however, are erratic when measuring ammonia.[13] Coupled-enzyme reactions are rapid, have a high specificity for ammonia, and are commonly used. One such reaction has been proposed as a candidate reference method.[14]

In the coupled-enzyme reaction, urease hydrolyzes urea into ammonia and carbon dioxide. Upon combining ammonia with 2-oxoglutarate and reduced nicotinamide adenine dinucleotide (NADH), the enzyme glutamate dehydrogenase (GLDH) oxidizes NADH to NAD^+.



The rate of change of the absorbance difference between 340 nm and 405 nm is caused by the conversion of NADH to NAD^+ and is directly proportional to the amount of urea present in the sample.

4. Principles of Procedure

See the Piccolo Xpress chemistry analyzer Operator's Manual, for the Principles and Limitations of the Procedure.

5. Description of Reagents

Reagents
Each Piccolo Kidney Check reagent disc contains dry test-specific reagent beads (described below). A dry sample blank reagent (comprised of buffer, surfactants, excipients, and preservatives) is included in each disc for use in calculating concentrations of urea nitrogen (BUN). A dedicated sample blank is included in the disc for creatinine (CRE). Each reagent disc also contains a diluent consisting of surfactants, excipients, and preservatives.

Table 1: Reagents

Component	Quantity/Disc
Adenosine-5'-diphosphate	8 µg
4-Aminoantipyrine-HCl (4-AAP)	27 µg
Ascorbate oxidase (*Cucurbita spp.*)	0.7 U
Creatine amidinohydrolase (*Actinobacillus spp*.)	6 U
Creatinine amidohydrolase (Pseudomonas *spp.*)	3 U
L-Glutamic acid dehydrogenase (bovine liver)	0.02 U
α-Ketoglutarate, disodium salt	47 µg
Lactate dehydrogenase (chicken heart)	0.003 U
Nicotinamide adenine dinucleotide, reduced (NADH)	13 µg
Peroxidase (horseradish)	1.4 U
Potassium ferrocyanide	0.9 µg
Sarcosine oxidase (microorganism)	1.4 U
2,4,6-Tribromo-3-hydroxybenzoic acid	376 µg
Urease (jack bean)	1 U
Buffers, surfactants, excipients, and preservatives	

Warnings and Precautions
- For *In vitro* Diagnostic Use

- The diluent container in the reagent disc is automatically opened when the analyzer drawer closes. A disc with an opened diluent container cannot be re-used. Ensure that the sample or control has been placed into the disc before closing the drawer.

- Used reagent discs contain human body fluids. Follow good laboratory safety practices when handling and disposing of used discs.[15] See the Piccolo Xpress chemistry analyzer Operator's Manual for instructions on cleaning biohazardous spills.

- The reagent discs are plastic and may crack or chip if dropped. **Never** use a dropped disc as it may spray biohazardous material throughout the interior of the analyzer.

- Reagent beads may contain acids or caustic substances. The operator does not come into contact with the reagent beads when following the recommended procedures. In the event that the beads are handled (e.g., cleaning up after dropping and cracking a reagent disc), avoid ingestion, skin contact, or inhalation of the reagent beads.

Instructions for Reagent Handling
Reagent discs may be used directly from the refrigerator without warming. Do not allow discs to remain at room temperature longer than 48 hours prior to use. Open the sealed foil pouch and remove the disc, being careful not to touch the bar code ring located on the top of the disc. Use according to the instructions provided in the Piccolo Xpress chemistry analyzer Operator's Manual. A disc not used within 20 minutes of opening the pouch should be discarded.

Storage
Store reagent discs in their sealed pouches at 2-8°C (36-46°F). Do not expose opened or unopened discs to direct sunlight or temperatures above 32°C (90°F). Reagent discs may be used until the expiration date included on the package. The expiration date is also encoded in the bar code printed on the bar code ring. An error message will appear on the Piccolo Xpress chemistry analyzer display if the reagents have expired.

Indications of Reagent Disc Instability/Deterioration
A torn or otherwise damaged pouch may allow moisture to reach the unused rotor and adversely affect reagent performance. Do not use a rotor from a damaged pouch.

6. Instrument

See the Piccolo Xpress chemistry analyzer Operator's Manual for complete information on use of the analyzer.

7. Sample Collection and Preparation

Sample collection techniques are described in the "Sample Collection" section of the Piccolo Xpress chemistry analyzer Operator's Manual.

- The minimum required sample size is ~100 µL of heparinized whole blood, heparinized plasma, serum or control material. The reagent disc sample chamber can contain up to 120 µL of sample.

- Whole blood samples obtained by venipuncture must be homogeneous before transferring a sample to the reagent disc. Gently invert the collection tube several times just prior to sample transfer. Do not shake the collection tube; shaking may cause hemolysis.

- Whole blood venipuncture samples should be run within 60 minutes of collection.[16]

- Refrigerating whole blood samples can cause significant changes in concentrations of **creatinine**.[17] The sample may be separated into plasma or serum and stored in capped sample tubes at 2-8°C (36-46°F) if the sample cannot be run within 60 minutes.

- Use only lithium heparin (green stopper) evacuated specimen collection tubes for whole blood or plasma samples. Use no-additive (red stopper) evacuated specimen collection tubes or serum separator tubes (red or red/black stopper) for serum samples.

- Start the test within 10 minutes of transferring the sample into the reagent disc.

8. Procedure

Materials Provided

- One Piccolo Kidney Check PN: 400-1033 (a box of discs PN: 400-0033)

Materials Required but not Provided

- Piccolo Xpress chemistry analyzer
- Sample transfer pipettes (fixed volume approximately 100 µL) and tips are provided with each Piccolo Xpress chemistry analyzer and may be reordered from Abaxis.
- Commercially available control reagents recommended by Abaxis (contact Abaxis Technical Service for approved control materials and expected values).
- Timer

Test Parameters
The Piccolo Xpress chemistry analyzer operates at ambient temperatures between 15°C and 32°C (59-90°F). The analysis time for each Piccolo Kidney Check reagent disc is less than 14 minutes. The analyzer maintains the reagent disc at a temperature of 37°C (98.6°F) over the measurement interval.

Test Procedure
The complete sample collection and step-by-step operating procedures are detailed in the Piccolo Xpress chemistry analyzer Operator's Manual.

Calibration
The Piccolo Xpress chemistry analyzer is calibrated by the manufacturer before shipment. The bar code printed on the bar code ring provides the analyzer with disc-specific calibration data. See the Piccolo Xpress chemistry analyzer Operator's Manual.

Quality Control
See Section 6 (Calibration and Quality Control) of the Piccolo Xpress chemistry analyzer Operator's Manual. Performance of the Piccolo Xpress chemistry analyzer can be verified by running controls. For a list of approved quality control materials with acceptance ranges, please contact Abaxis Technical Support. Other human serum or plasma-based controls may not be compatible. Quality control materials should be stored as per the package-insert included with the controls.

If control results are out of range, repeat one time. If still out of range, call Technical Support. Do not report results if controls are outside their labeled limits. See the Piccolo Xpress chemistry analyzer Operator's Manual for a detailed discussion on running, recording, interpreting, and plotting control results.

Waived Laboratories: Abaxis recommends control testing as follows:

- at least every 30 days
- whenever the laboratory conditions have changed significantly, e.g. Piccolo moved to a new location or changes in temperature control
- when training or retraining of personnel is indicated
- with each new lot (CLIA waived tests in waived status labs)

Non-Waived Laboratories: Abaxis recommends control testing to follow federal, state, and local guidelines.

9. Results

The Piccolo Xpress chemistry analyzer automatically calculates and prints the analyte concentrations in the sample. Details of the endpoint and rate reaction calculations are found in the Piccolo Xpress chemistry analyzer Operator's Manual.

Interpretation of results is detailed in the Operator's Manual. Results are printed onto result cards or paper rolls supplied by Abaxis. The result cards or paper rolls have an adhesive backing for easy placement in the patient's files.

10. Limitations of Procedure

General procedural limitations are discussed in the Piccolo Xpress chemistry analyzer Operator's Manual**.**

- The only anticoagulant **recommended for use** with the Piccolo Xpress chemistry analyzer system is **lithium heparin**. Do not use sodium heparin.

- Abaxis has performed studies demonstrating that EDTA, fluoride, oxalate, and any anticoagulant containing ammonium ions will interfere with at least one chemistry contained in the Piccolo Kidney Check reagent disc.

- Samples with hematocrits in excess of 62-65% packed red cell volume (a volume fraction of 0.62-0.65) may give inaccurate results. Samples with high hematocrits may be reported as hemolyzed. These samples may be spun down to get plasma then re-run in a new reagent disc.

- **Any result for a particular test that exceeds the assay range should be analyzed by another approved test method or sent to a referral laboratory. Do not dilute the sample and run it again on the Piccolo Xpress chemistry analyzer.**

  Warning: Extensive testing of the Piccolo Xpress chemistry analyzer has shown that, in very rare instances, sample dispensed into the reagent disc may not flow smoothly into the sample chamber. Due to the uneven flow, an inadequate quantity of sample may be analyzed and several results may fall outside the reference ranges. The sample may be re-run using a new reagent disc.

Interference
Substances were tested as interferents with the analytes. Human serum pools were prepared. The concentration at which each potential interferent was tested was based on the testing levels in CLSI EP7-P.[18]

Effects of Endogenous Substances

- Physiological interferents (hemolysis, icterus and lipemia) cause changes in the reported concentrations of some analytes. The sample indices are printed on the bottom of each printout to inform the operator about the levels of interferents present in each sample.

- The Piccolo Xpress chemistry analyzer suppresses any results that are affected by >10% interference from hemolysis, lipemia or icterus. “HEM”, “LIP”, or “ICT” respectively, is printed on the printout in place of the result.

- For maximum levels of endogenous substances contact Abaxis Technical Support.

Effects of Exogenous and Therapeutic Substances

- Thirty-five exogenous and therapeutic substances were selected as potential interferents for Abaxis test methods based on recommendations by Young.[19] Significant interference is defined as a >10% shift in the result for a normal range specimen. Human serum pools were supplemented with a known concentration of the drugs or chemicals and then analyzed.

Table 2: Exogenous & Therapeutic Substances Evaluated

Potential Interferents	Highest Concentration Tested (mg/dL)
Acetaminophen	100
Acetoacetate	102
Acetylsalicylic Acid	50
Ampicillin	30
Ascorbic acid	20
Caffeine	10
Calcium Chloride	20
Cephalothin (Keflin)	400
Chloramphenicol	100
Cimetidine	16
Dopamine	19
Epinephrine	1
Erythromycin	10
Glutathione	30
Hydrochlorothiazide	7.5
Ibuprofen	50
Isoniazide	4
α-Ketoglutarate	5
Ketoprofen	50
L-dopa	5
Lidocaine	1
Lithium Lactate	84
Methicillin	100
Methotrexate	0.5
Metronidazole	5
Nafcillin	1
Nitrofurantoin	20
Oxacillin	1
Oxaloacetate	132
Penicillin G	100
Phenytoin (5,5-Diphenylhydantion)	3
Proline	4
Pyruvate	44
Rifampin	0.5
Salicylic Acid	50
Sulfadiazine	150
Sulfanilamide	50
Theophylline	20

- The following substances showed greater than 10% interference. Significant interference is defined as >10% shift in the result for a normal range specimen. Human serum pools were supplemented with known concentrations of the drugs or chemicals and then analyzed.

Table 3: Substances With Significant Interference >10%

	Concentration Which Produces > 10% Interference	% Interference Observed
Creatinine (CRE)		
Ascorbic acid	20	11% dec*
Dopamine	19	80% dec
L-dopa	5	71% dec
Epinephrine	1	45% dec
Glutathione	30	13% dec

*dec=decrease.

For additional information on potential chemical interferents, see the Bibliography.

11. Expected Values

Samples from a total of 193 adult males and females, analyzed on the Piccolo blood chemistry analyzer, were used to determine the reference ranges for creatinine and BUN. These ranges are provided as a guideline only. It is recommended that your office or institution establish normal ranges for your particular patient population.

Table 4: Piccolo Reference Intervals

Analyte	Common Units	SI Units
Creatinine (CRE)	0.6-1.2 mg/dL	53-106 µmol/L
Blood Urea Nitrogen (BUN)	7-22 mg/dL	2.5-7.9 mmol urea/L

12. Performance Characteristics

Linearity
The chemistry for each analyte is linear over the dynamic range listed below when the Piccolo Xpress chemistry analyzer is operated according to the recommended procedure (refer to the Piccolo Xpress chemistry analyzer Operator's Manual).

Table 5: Piccolo Dynamic Ranges

Analyte	Common Units	SI Units
Creatinine (CRE)	0.2-20 mg/dL	18-1768 µmol/L
Blood Urea Nitrogen (BUN)	2-180 mg/dL	0.7-64.3 mmol urea/L

If the analyte concentration is above the measuring range (dynamic range), but less than the system range, the printout will indicate a ">" sign at the upper limit and an asterisk after the number, e.g. CRE >20* mg/dL. If lower than the dynamic range, a "<" will be printed with an asterisk, e.g. CRE <0.2* mg/dL. For values that are grossly beyond the measurement range (system range), "~~~" will be printed instead of a result. Any time "~~~" appears on a printout, collect a new sample and rerun the test. If results for the second sample are suppressed again, please call Abaxis Technical Support.

Sensitivity (Limits of Detection)
The lower limit of the reportable (dynamic) range for each analyte is: creatinine 0.2 mg/dL (18 µmol/L) and urea nitrogen 2.0 mg/dL (0.7 mmol urea/L).

Precision
Precision studies were conducted using CLSI EP5-T2 guidelines.[20] Results for within-run and total precision were determined by testing two levels of control material. Controls were run in duplicate twice each day for 20 days over a four-week period. Results of the precision studies are shown in Table 6.

Table 6: Precision (N=80)

Analyte	Within-Run	Total
Creatinine (mg/dL)		
Control Level 1		
Mean	1.1	1.1
SD	0.14	0.14
%CV	12.5	13.1
Control Level 2		
Mean	5.2	5.2
SD	0.23	0.27
%CV	4.4	5.2
Blood Urea Nitrogen (mg/dL)		
Control Level 1		
Mean	19	19
SD	0.35	0.40
%CV	1.9	2.1
Control Level 2		
Mean	65	65
SD	1.06	1.18
%CV	1.6	1.8

Correlation

Heparinized whole blood and serum samples were collected from patients at two sites. The whole blood samples were analyzed by the Piccolo blood chemistry analyzer at the field sites and the serum samples were analyzed by comparative methods. In some cases, high and low supplemented samples were used to cover the dynamic range. All samples were run in singlicate on the same day. Representative correlation statistics are shown in Table 7.

Table 7: Correlation of Piccolo blood chemistry analyzer with Comparative Methods

	Correlation Coefficient	Slope	Intercept	SEE	N	Sample Range	Comparative Method
Creatinine (mg/dL)	0.993	0.926	0.0	0.15	260	0.4-14.7	Paramax
	0.987	0.866	0.1	0.16	107	0.4-7.5	Beckman
Blood Urea Nitrogen (mg/dL)	0.964	0.923	0.5	1.08	251	6-52	Paramax
	0.983	0.946	0.0	0.66	92	6-38	Beckman

Results of Untrained User Study

An "untrained user" study was conducted in which participants were given only the test instructions and asked to perform testing of 3 discs with blinded randomized samples. The samples consisted of serum pools prepared at three levels for each of the analytes. The participants were not given any training on the use of the test. A total of approximately 60 participants were enrolled from 3 sites, representing a diverse demographic (educational, age, gender, etc) population.

Tables below present the summary of the performance for each analyte.

Creatinine (CRE)

	Level 1	Level 2	Level 3
N	62	62	62
Mean	0.89	2.07	6.89
%CV	11.0	5.0	1.6
Observed Range	0.7 – 1.2	1.8 – 2.3	6.5 – 7.2
Percent of Results	93.6	100%	100%

in the Range ± 15.0%*	58/62 95%CI: 84.3% to 98.2%	62/62 95%CI: 94.2% to 100%	62/62 95%CI: 94.2% to 100%

* This percent is based on the premise that one cannot distinguish properly between normal and abnormal values when errors are greater than one-quarter of the normal range. The range of (0.6 mg/dL – 1.2 mg/dL) was considered.

Blood Urea Nitrogen (BUN)

	Level 1	Level 2	Level 3
N	62	62	62
Mean	15.1	41.0	72.2
%CV	2.3	2.5	1.8
Observed Range	14 – 16	37 – 43	68 – 75
Percent of Results in the Range ± 15.0%	100% 62/62 95%CI: 94.2% to 100%	100% 62/62 95%CI: 94.2% to 100%	100% 62/62 95%CI: 94.2% to 100%

13. Symbols


Use By

Catalog Number

Batch Code

In Vitro Diagnostic Medical Device


Consult Instructions For Use


Manufacturer


Do Not Reuse


X Number of Test Devices in Kit

Manufacturing Sequence

Serial Number


Caution


Temperature Limitation

PN:
Part Number

Authorized Representative In the European Community


Denotes conformity to specified European directives

UDI Barcode structure in Health Industry Bar Code (HIBC) standard format

Unique Device Identifier (UDI) in human and machine-readable form used to adequately identify medical devices through their distribution and use


Separate waste collection for this electronic item indicated; Equipment manufactured / placed on the market after 13 August 2005; Indicates compliance with Article 14(4) of Directive 2012/19/EU (WEEE) for the European Union (EU).

14. Bibliography

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