CLINITEK® Microalbumin

Reagent Strips for Determining Albumin and Creatinine in Urine

For instrumental use only

SUMMARY AND EXPLANATION / INTENDED USE: CLINITEK® Microalbumin Reagent Strips are firm plastic strips that contain two reagent areas that test for albumin and creatinine in urine. An albumin-to-creatinine ratio is also determined, which allows for the use of single-void specimens in testing. The ratio is given in milligrams albumin per gram or millimole creatinine (mg/g or mg/mmol). This product provides semi-quantitative results and can be used for screening samples for microalbuminuria; positive results should be confirmed with quantitative methods for albumin.

Test results may aid clinicians in the detection of patients at risk of developing kidney damage. Microalbuminuria has been reported to be an early predictor of the development of glomerular damage in the absence of overt nephropathy.[1-3] Patients with diabetes and hypertension are the primary risk groups. Patients who have been exposed to nephrotoxins or who suffer from immune disorders form the secondary risk groups; microalbuminuria has also been reported as an early predictor of the development of preeclampsia during pregnancy.[4]

The reagent test areas on CLINITEK Microalbumin Reagent Strips are ready to use upon removal from the bottle and the entire reagent strip is disposable. The strips are read instrumentally, using the CLINITEK STATUS®, CLINITEK® 50, or CLINITEK® 100 Urine Chemistry Analyzer and the appropriate software (version 4.00 and higher with the CLINITEK 50 Analyzer and version 6.00 and higher with the CLINITEK 100 Analyzer). The instrument automatically identifies the strip being tested, using the colored bands near the handle of the strip.

The directions must be followed exactly. The reagent strips must be kept in the bottle with the cap tightly closed to maintain reagent reactivity. To obtain optimal results, testing should be done on FRESH urine.

INFORMATION REGARDING CLIA WAIVER (U.S. ONLY):

- The CLINITEK STATUS and CLINITEK 50 Analyzers are CLIA waived only when used with Bayer Reagent Strips, manufactured by Bayer HealthCare LLC.
- CLINITEK Microalbumin Strips are CLIA waived when run on the CLINITEK STATUS and CLINITEK 50 Analyzers. A certificate of CLIA waiver is required to perform these tests in a waived setting. To obtain a Certificate of Waiver, contact your state department of health or visit the CMS web site for an application, Form CMS-116.
- Failure to adhere to the instructions for use, including instructions for limitations, intended use, and performing quality control testing, is off-label use, resulting in these tests being categorized as high complexity and subject to all CLIA regulations.

CHEMICAL PRINCIPLES OF PROCEDURES:

Albumin: This test is based on dye binding using a high affinity sulfonephthalein dye. At a constant pH, the development of any blue color is due to the presence of albumin. The resulting color ranges from pale green to aqua blue.

Creatinine: This test is based on the peroxidase-like activity of a copper creatinine complex that catalyzes the reaction of diisopropylbenzene dihydroperoxide and 3,3',5,5'-tetramethylbenzidine. The resulting color ranges from orange through green to blue.

REAGENTS: (based on dry weight at time of impregnation)

Albumin: 1.9% w/w bis (3',3"-diiodo-4',4"-dihydroxy-5',5"-dinitrophenyl)-3,4,5,6-tetrabromosulfonephthalein; 94.2% w/w buffer; 3.9% w/w nonreactive ingredients.

Creatinine: 2.5% w/w copper sulfate; 4.5% w/w diisopropylbenzene dihydroperoxide; 2.0% w/w 3,3',5,5'-tetramethylbenzidine; 56.4% w/w buffer; 34.6% w/w nonreactive ingredients.

WARNINGS AND PRECAUTIONS: CLINITEK Microalbumin Reagent Strips are for *in vitro* diagnostic use. They have been determined to be nonhazardous under the guidelines issued by OSHA in 29 CFR 1910.1200(d).

STORAGE: Store at room temperature between 15°–30°C (59°–86°F). Do not use product after expiration date. Do not store the bottle in direct sunlight.

PROCEDURES FOR HANDLING CLINITEK MICROALBUMIN: All unused strips must remain in the original bottle. Transfer to any other container may cause reagent strips to deteriorate and become unreactive. Do not remove desiccant packet(s) from bottle. **Remove each strip from the bottle immediately before it is to be used for testing. Replace cap immediately and tightly after removing reagent strip.** Do not touch test areas of the reagent strip. Work areas and specimen containers should be free of detergents and other contaminating substances. Dip test areas in urine completely, but briefly, to avoid dissolving out the reagents.

IMPORTANT: PROTECTION AGAINST AMBIENT MOISTURE, LIGHT AND HEAT IS ESSENTIAL TO GUARD AGAINST ALTERED REAGENT REACTIVITY. Discoloration or darkening of reagent areas may indicate deterioration. If this is evident, or if test results are questionable or inconsistent with expected findings, the following steps are recommended: (1) confirm that the product is within the expiration date shown on the label; (2) check performance against known positive and negative control materials; (3) retest with fresh product. If proper results are not obtained, consult your local Bayer representative, or contact the Technical Care Center by calling toll free (1-877-229-3711 in U.S.A.; 1-800-268-1432 in Canada), for advice on testing technique and results.

SPECIMEN COLLECTION AND PREPARATION: Test the urine specimen as soon as possible. Boric acid, at a concentration of 1.0 g/L, is the only urine preservative that is recommended. If testing cannot be done within two hours after voiding, refrigerate the specimen immediately and let it return to room temperature before testing. Prolonged exposure of unpreserved urine to room temperature may result in microbial proliferation with resultant loss of albumin. Specimens may be stored at 0° to 8°C for one week or at −20°C for one month without significant effect on results with this test.

Any single-void urine specimen, when evaluated in conjunction with the albumin-to-creatinine ratio, can be used to discriminate between normal and abnormal levels of microalbuminuria.[5-7] First-morning specimens are recommended.[8] Urinary albumin fluctuates day-to-day; therefore, testing three urine samples over a three-to-six month period may increase the predictive value, where two positive samples are predictive of incipient nephropathy.[2, 7] Twenty-four hour or timed collections may also be used with this test to determine the albumin excretion rate (AER). Additional information on screening guidelines is available from the American Diabetes Association Position Statement.[7]

It is suggested that you screen the urine for protein, using a Bayer Reagent Strip such as MULTISTIX® 10 SG. Urines showing a result of 30 mg/dL (0.3 g/L) or greater for protein or that are visibly bloody should not be tested using CLINITEK Microalbumin Reagent Strips.

Contamination of the urine specimen with soaps, detergents, antiseptics, or skin cleansers may affect test results. The user should determine whether the use of such products is warranted.

PROCEDURE: MUST BE FOLLOWED EXACTLY TO ACHIEVE RELIABLE TEST RESULTS.

1. **Collect** a FRESH urine specimen in a clean, dry container.
2. **Remove** one strip from bottle and replace the cap tightly.
3. **CLINITEK STATUS only: Touch** the word "START."
4. **Dip** the test pads into the urine, making sure both pads are wetted. (Do not dip the colored bands near the handle.)
5. **Immediately remove** the strip, dragging the edge of the strip against the rim of the urine container to remove excess urine.
6. **CLINITEK 50 and CLINITEK 100 Analyzers only: Press** the green ◊ key (START) **at the same time** as the strip is removed from the urine.
7. **Blot** the strip by **touching the edge only** to a paper towel.
8. **Place** the reagent strip, **with the reagent pads facing up,** onto the instrument's test/feed table. Slide the strip along the table until it touches the **end** of the table.
9. The table is automatically pulled into the instrument, where the strip is identified and read. Results are displayed or printed as soon as they are available.
10. **Record** the results you obtain, then discard the strip into a suitable trash container.

    NOTE: Wipe the test table with a damp, lint-free tissue as often as needed to prevent urine from building up.

QUALITY CONTROL:

CLIA Waived laboratories (U.S. only): Test negative and positive controls whenever a new reagent bottle is opened. Liquid, ready-to-use controls should be used. Water should not be used as a negative control. Compare control results to those listed as acceptable by the manufacturer of the control material. If control results are not acceptable, do not test patient samples until the problem is resolved and repeat control results are acceptable. For assistance, call the Bayer Technical Care Center at 1-877-229-3711 (U.S. only).

All other laboratories: For best results, confirm performance of reagent strips at the start of each day and whenever a new bottle is first opened by testing with commercially-available negative and positive controls that

include values for microalbumin and creatinine. These control specimens may also be randomly hidden in each batch of specimens tested. Each laboratory should establish its own goals for adequate standards of performance, and should question handling and testing procedures if these standards are not met. For information about control manufacturers, contact the Bayer Technical Care Center at 1-877-229-3711 (U.S. only).

LIMITATIONS OF PROCEDURES: As with all laboratory tests, definitive diagnostic or therapeutic decisions should not be based on any single result or method.

The presence of hemoglobin or myoglobin (≥5 mg/dL or a visibly bloody urine) may cause falsely elevated results with both the albumin and creatinine tests. Contamination of the urine specimen with soaps, detergents, antiseptics, or skin cleansers, or the use of urine preservatives other than boric acid (1.0 g/L), may also affect test results. The presence of cimetidine (Tagamet) may cause falsely elevated results with the creatinine test.

Substances that cause abnormal urine color, such as drugs containing azo dyes (e.g., Pyridium, Azo Gantrisin, Azo Gantanol), nitrofurantoin (Macrodantin, Furadantin), and riboflavin, may affect the readability of the reagent areas on urinalysis reagent strips. The color development on the reagent pad may be masked, or a color reaction may be produced on the pad that could be interpreted as a false positive.

TABLE OF RESULTS: The following table shows the results, in both conventional and SI units, that can be obtained when using the CLINITEK Analyzer:

Test	Abbreviation	Printed / Displayed Results			
		Conventional		S.I. Units	
Albumin	ALB	10 mg/L	80 mg/L	10 mg/L	80 mg/L
		30 mg/L	150 mg/L	30 mg/L	150 mg/L
Creatinine	CRE	10 mg/dL	200 mg/dL	0.9 mmol/L	17.7 mmol/L
		50 mg/dL	300 mg/dL	4.4 mmol/L	26.5 mmol/L
		100 mg/dL		8.8 mmol/L	
Albumin-to-Creatinine Ratio	A:C	<30 mg/g (Normal)		<3.4 mg/mmol (Normal)	
		30–300 mg/g (Abnormal)		3.4–33.9 mg/mmol (Abnormal)	
		>300 mg/g (High Abnormal)		>33.9 mg/mmol (High Abnormal)	

Shaded areas = abnormal results

EXPECTED VALUES:

Albumin: Albumin is normally present in urine at concentrations of less than 20 mg/L.[9] Microalbuminuria is indicated with results of 20–200 mg/L; results of >200 mg/L indicate clinical albuminuria. These levels have been found to be predictive of albumin excretion rates of 30–300 mg/24 hours and >300 mg/24 hours, respectively.[10] Urinary albumin excretions can be temporarily elevated by exercise, urinary tract infections, and acute illness with fever.

Creatinine: Creatinine is normally present in urine at concentrations of 10 to 300 mg/dL (0.9 to 26.5 mmol/L).

Albumin-to-Creatinine Ratio: Albumin is normally present in urine at concentrations of less than 30 mg albumin/g creatinine (3.4 mg albumin/mmol creatinine). Microalbuminuria is indicated at a ratio result of 30–300 mg/g (3.4–33.9 mg/mmol) (Abnormal) and clinical albuminuria at a ratio result of >300 mg/g (>33.9 mg/mmol) (High Abnormal).[7]

SPECIFIC PERFORMANCE CHARACTERISTICS: Specific performance characteristics are based on clinical and analytical studies. In clinical specimens, the sensitivity of the reagent tests and their respective reference assays depends upon the presence or absence of inhibitory factors typically found in urine (see LIMITATIONS OF PROCEDURES section).

Each instrumental result represents a range of values. Because of specimen variability, specimens with analyte concentrations that fall between nominal levels may give results at either level.

The performance characteristics of the CLINITEK Microalbumin test on the CLINITEK STATUS, CLINITEK 50, and CLINITEK 100 Analyzers was determined at multiple hospital clinical laboratories with urine specimens from patients presenting for routine urinalysis. CLINITEK instrument albumin results were compared to the results obtained with a commercially-available immunoassay test; the creatinine results were compared to a kinetic Jaffe creatinine assay.

The following table shows the results of the testing. Accuracy is defined as the agreement between the CLINITEK instrument/reagent system and the comparative methods. Positive percent agreement is defined as the percentage of positive results obtained by the instrument/reagent system relative to those obtained by the comparative methods, while negative percent agreement refers to the percentage of negative results.

Albumin Test Pad with:	Accuracy	Percent Agreement Positive	Percent Agreement Negative
CLINITEK STATUS	85% n = 1633	86% n = 1195	82% n = 438
CLINITEK 50	87% n = 1544	90% n = 779	84% n = 765
CLINITEK 100	85% n = 1596	83% n = 798	87% n = 798

Albumin-to-Creatinine Ratio with:	Accuracy	Percent Agreement Positive	Percent Agreement Negative
CLINITEK STATUS	86% n = 1541	81% n = 741	90% n = 800
CLINITEK 50	86% n = 1544	86% n = 721	87% n = 823
CLINITEK 100	85% n = 1596	83% n = 738	86% n = 858

Albumin: In contrived urine, the albumin test generally detects albumin at a concentration of 20–40 mg/L; because of the inherent variability of clinical urines, lesser concentrations may be detected under certain conditions. The test is specific for albumin and is not affected by the following proteins when tested at concentrations at least nine times greater than the excretion rate considered to be abnormal:[11]

- lysozyme
- prealbumin
- immunoglobulins
- haptoglobin
- transferrin
- Bence-Jones protein
- Tamm Horsfall glycoprotein
- β_2-microglobulin
- β_2-glycoprotein
- α_1-acid glycoprotein
- α_1-microglobulin
- α_1-antitrypsin
- retinol binding protein

Creatinine: This test area detects urinary creatinine in concentrations as low as 10 mg/dL (0.9 mmol/L); the absence of creatinine in a specimen cannot be determined.

Albumin-to-Creatinine Ratio: In contrived urines, the ratio generally detects 30–300 mg/g (3.4–33.9 mg/mmol) albumin-to-creatinine.

AVAILABILITY: CLINITEK Microalbumin Reagent Strips for Urinalysis are available in bottles of 25 strips as Product #2083.

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