Multistix® 10 SG • Multistix® 9 • Multistix® 9 SG • Multistix® 8 SG • Multistix® 7 • Multistix® • Labstix® Reagent Strips

Tests for Protein, Blood, Leukocytes, Nitrite, Glucose, Ketone (Acetoacetic Acid), pH, Specific Gravity, Bilirubin and Urobilinogen in Urine.

INTENDED USE:

Siemens Healthcare Diagnostics Reagent Strips for Urinalysis include test pads for protein, blood, leukocytes, nitrite, glucose, ketone (acetoacetic acid), pH, specific gravity, bilirubin and urobilinogen. Please refer to the carton or bottle label to see which tests are included on the product you are using.

Siemens Reagent Strips are for professional *in vitro* diagnostic use in near-patient (point of care) and centralized laboratory locations. The strips are intended for use in at-risk patient groups to assist diagnosis in the following areas:[1-3]

- kidney function
- urinary tract infections
- carbohydrate metabolism (e.g., diabetes mellitus)
- liver function

The strips also measure physical characteristics, including acid-base balance and urine concentration. Test results can be used along with other diagnostic information to rule out certain disease states and to determine if microscopic analysis is needed.[1,4]

SUMMARY AND EXPLANATION:

Siemens Reagent Strips are ready to use upon removal from the bottle and the reagent strip is disposable. The strips may be read visually, requiring no additional laboratory equipment for testing. The strips can also be read instrumentally, using the CLINITEK® family of Urine Chemistry Analyzers and the appropriate software; contact your product representative for further information. Siemens Reagent Strips with ID bands provide Auto-Checks when read on select CLINITEK instruments. Auto-Checks include automatic strip identification and quality checks. Siemens Reagent Strips have been determined to be nonhazardous under the guidelines issued by OSHA in 29 CFR 1910.1200(d).

INFORMATION REGARDING CLIA WAIVER:

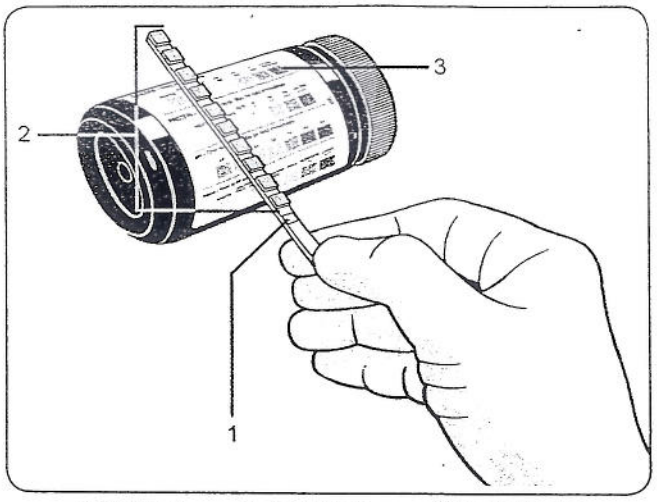
- The CLINITEK STATUS systems and CLINITEK 50 Analyzers are CLIA waived only when used with Siemens Reagent Strips, manufactured by Siemens.
- These tests are CLIA waived when read visually and when run on the CLINITEK STATUS systems and CLINITEK 50 Analyzers. A certificate of CLIA waiver is required 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.

SPECIMEN COLLECTION AND PREPARATION: Collect freshly-voided urine in a clean container and test it as soon as possible. The container should allow for complete dipping of all reagent strip areas. A first-morning specimen is preferred but random collections are acceptable. Test the urine within two hours after voiding. If unable to test within the recommended time, refrigerate the specimen immediately and let it return to room temperature, between 15–30°C (59–86°F), before testing. The use of urine preservatives is not recommended.

CAUTION: Ensure that work areas and specimen containers are always free of detergents and other contaminants. Some substances can interfere with patient results. Contamination of the urine specimen with skin cleansers containing chlorhexidine may affect protein test results. The user should determine whether the use of such cleansers is warranted.

Procedure

1. Collect a fresh urine specimen in a clean, dry container.
2. Mix well just before testing, but do not centrifuge.
3. Check the expiration date on the Reagent Strip bottle. If the date has passed, discard and get a new bottle. Record the opening date on the label.
   Use of Reagent Strips beyond the expiration date may yield inaccurate results.
4. Remove a strip from the bottle and replace the cap.
   NOTE: Do not touch the test pads on the strip.
5. Dip all the test pads of the strip into the urine and immediately remove the strip. If reading the strip visually, start timing.
   NOTE: The ID band can be dipped into urine and controls solutions.
6. Drag the edge of the strip against the container rim to remove excess urine and blot the edge on a paper towel or tissue if using the CLINITEK 50 or CLINITEK Status Analyzers. It is not necessary to blot if reading visually or using the CLINITEK Advantus Analyzer.
7. **If reading visually:**
   - **Compare** each test pad to the corresponding row of color blocks on the bottle label.
   - **Read** each pad at the time shown on the label, starting with the shortest time.
   - **Hold** the strip close to the color blocks and match carefully.
   - **Read** the pads in good light.



1. ID Band **2. Test Pads** **3. Color Block**

If using an analyzer, place the test strip on the analyzer according to the analyzer operating manual. The analyzer automatically reads each test pad at a specified time.

HELPFUL HINTS: Discoloration or darkening of the test pads may indicate deterioration. If this is evident, or if test results are 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 negative and positive control materials.
3. Retest with fresh product.

RESULTS: With visual use, results are obtained in clinically meaningful units directly from the Color Chart comparison. **With CLINITEK instruments,** the test pads are "read" by the instrument and the results are displayed or printed as soon as they are available.

QUALITY CONTROL: Test negative and positive controls when you first open a new bottle. Water should NOT be used as a negative control. Each laboratory should establish its own goals for adequate standards of performance. CHEK-STIX® Positive and Negative Control Strips provide a convenient basis for a quality control program.

CLIA-WAIVED LABORATORIES:

Test positive and negative quality controls with new lots, new shipments of reagents, and when you open a new bottle of reagent strips. Test reagents monthly that are stored for more than 30 days.

Run QC tests to ensure reagent strips integrity; train new users; confirm test performance; and when patients' clinical conditions or symptoms do not match. Also, run QC tests per your laboratory procedures. Liquid ready-to-use controls are available. Do not use water as a negative control. For recommendations and technical questions, call Technical Support at 877-229-3711 or visit www.siemens.com/diagnostics.

Compare QC results to the QC manufacturer's acceptable results list. If the QC results are not acceptable, do not test the patient samples until you solve the problem. Repeat QC tests until you have acceptable results.

STORAGE: All unused strips must remain in the original bottle. Transfer to any other container may cause reagent strips to deteriorate and become unreactive. Store at temperatures between 15–30°C (59–86°F). Do not use the strips after their expiration date. Do not store the bottle in direct sunlight and do not remove the desiccant from the bottle.

IMPORTANT NOTE: PROTECTION AGAINST EXPOSURE TO LIGHT, HEAT AND AMBIENT MOISTURE IS MANDATORY TO GUARD AGAINST ALTERED REAGENT REACTIVITY.

REAGENT PERFORMANCE:

Expected values for the "normal" healthy population and the abnormal population are listed below for each reagent.

Sensitivities listed for each reagent are the generally detectable levels of the analytes in contrived urines; however, because of the inherent variability of clinical urines, lesser concentrations may be detected under certain conditions. The percentage of clinical specimens correctly detected as positive increases with analyte concentration.

Performance characteristics are based on clinical and analytical studies and depend upon several factors: the variability of color perception; the presence or absence of inhibitory and matrix factors typically found in urine; and the laboratory conditions in which the product is used (e.g., lighting, temperature, and humidity). The strips should be read in good light, such as fluorescent; do not read in direct sunlight.

Each color block or instrumental result represents a range of values. Because of specimen and reading variability, specimens with analyte concentrations that fall between nominal levels may give results at either level. Results will usually be within one level of the true concentration. Exact agreement between visual results and instrumental results might not be found because of the inherent differences between the perception of the human eye and the optical systems of the instruments.

Limitations given for the reagents include specific substances and conditions that may affect the test results. **As with all laboratory tests, definitive diagnostic or therapeutic decisions should not be based on any single result or method.**

Substances that cause abnormal urine color may affect the readability of test pads on urinalysis reagent strips. These substances include visible levels of blood or bilirubin and drugs containing dyes (e.g., Pyridium®, Azo Gantrisin®, Azo Gantanol®), nitrofurantoin (Macrodantin®, Furadantin®), or riboflavin. Levels of ascorbic acid normally found in urine do not interfere with these tests.

PROTEIN [PRO] :

Expected values: Protein in urine can be the result of urological and nephrological disorders. In normal urine, less than 150 mg of total protein is excreted per day (24 hour period) (< 15 mg/dL). Clinical proteinuria is indicated at greater than 500 mg of protein per day (strip result of ≥ 30 mg/dL). Positive results may also indicate tubular or overflow proteinuria in the absence of any glomerular abnormality or proteins of renal origin that may be excreted during infection. Urinary protein excretions can be temporarily elevated in the absence of renal abnormality by strenuous exercise, orthostatic proteinuria, dehydration, urinary tract infections, and acute illness with fever.[1,6-7] Clinical judgment is needed to evaluate the significance of Trace results.

Sensitivity: 15–30 mg/dL albumin

Performance characteristics: The protein test pad is not specific for a particular protein, and proteins other than albumin can cause a positive response. The test is less sensitive to mucoproteins and globulins, which are generally detected at levels of 60 mg/dL or higher.[8]

Limitations: A visibly bloody urine may cause falsely elevated results.[8]

BLOOD [BLO] :

Expected values: Normally, no hemoglobin is detectable in urine (< 0.010 mg/dL or 3 RBC/µL). Occult blood occurs in urine as intact erythrocytes and hemoglobin, which can occur during urological, nephrological and bleeding disorders. Small amounts of blood (0.030–0.065 mg/dL or a strip result of Small) are sufficiently abnormal to require further investigation. The significance of the Trace reaction may vary among patients, and clinical judgment is required for assessment in an individual case. Blood is often, but not always, found in the urine of menstruating females.[1,9]

Sensitivity: 0.015–0.062 mg/dL hemoglobin

Performance characteristics: The appearance of green spots on the reacted test pad indicates the presence of intact erythrocytes, while green color across the entire test pad indicates free hemoglobin. The test is equally sensitive to myoglobin as to hemoglobin. This test complements the microscopic examination; a hemoglobin concentration of 0.015–0.062 mg/dL is approximately equivalent to 5–20 intact red blood cells per microliter.

Limitations: Capoten® (captopril) may reduce the sensitivity. Certain oxidizing contaminants, such as hypochlorite, may produce false positive results. Microbial peroxidase associated with urinary tract infection may cause a false positive reaction.

LEUKOCYTES [LEU] :

Expected values: Normal urine specimens generally yield negative results. An increase in leukocytes (≥ 10 leukocytes/µL) is an indication of pyuria and is found in nearly all diseases of the kidney and urinary tract; however, pyuria may often be present in non-infective conditions.[1] A strip result of Small or greater is a useful indicator of infection. Trace results may be of questionable clinical significance; however, Trace results observed repeatedly may be clinically significant.

Sensitivity: 5–15 white blood cells/hpf in clinical urine.

Performance characteristics: Leukocyte esterase is a reliable indicator of leukocytes in urine.[1] A positive reaction (Small or greater) at less than the 2 minute reading time may be regarded as a positive indication of leukocytes in urine.

Limitations: Elevated glucose concentrations (≥ 3 g/dL) may cause decreased test results. The presence of cephalexin (Keflex®), cephalothin, or high concentrations of oxalic acid may also cause decreased test results. Tetracycline may cause decreased reactivity, and high levels of the drug may cause a false negative reaction. Positive results may occasionally be due to contamination of the specimen by vaginal discharge.

NITRITE [NIT] :

Expected values: Normally no nitrite is detectable in urine. Many enteric gram-negative organisms give positive results when their number is greater than 10^5/mL (0.075 mg/dL nitrite ion or greater).[2]

Sensitivity: 0.06–0.1 mg/dL nitrite ion.

Performance characteristics: The test is specific for nitrite and will not react with any other substance normally excreted in urine. Nitrite concentration during infection increases with the length of time the urine specimen is retained in the bladder prior to collection. A minimum of four hours of bladder incubation significantly increases the likelihood of obtaining a positive result.

Limitations: Pink spots or pink edges should not be interpreted as a positive result. A negative result does not rule out significant bacteriuria. False negative results may occur with shortened bladder incubation of the urine, absence of dietary nitrate, or the presence of nonreductive pathological microbes.

GLUCOSE [GLU] :

Expected values: Small amounts of glucose (< 30 mg/dL) are normally excreted by the kidney. These amounts are usually below the sensitivity level of this test but on occasion may produce a result between Negative and 100 mg/dL that is interpreted as a positive result. Results at the first positive level may be significantly abnormal if found consistently.[2]

Sensitivity: 75–125 mg/dL glucose

Performance characteristics: The test is specific for glucose; no substance excreted in urine other than glucose is known to give a positive result. This test may be used to determine whether the reducing substance found in urine is glucose. If the color appears somewhat mottled at the higher glucose concentrations, match the darkest color to the color blocks.

Limitations: Ketone bodies reduce the sensitivity of the test; moderately high ketone levels (40 mg/dL) may cause false negatives for specimens containing small amounts of glucose (75–125 mg/dL) but the combination of such ketone levels and low glucose levels is metabolically improbable in screening.

KETONE [KET] :

Expected values: Normally, no ketone is detectable in urine (up to 2 mg/dL acetoacetic acid). In ketoacidosis, starvation or with other abnormalities of carbohydrate or lipid metabolism, ketones may appear in urine at levels of 10 mg/dL or higher before serum ketone levels are elevated. Clinical judgment is needed to determine the significance of Trace results, which may occur during physiological stress conditions such as fasting, pregnancy and frequent strenuous exercise.[1]

Sensitivity: 5–10 mg/dL acetoacetic acid

Performance characteristics: The test reacts with acetoacetic acid in urine. It does not react with acetone or β-hydroxybutyric acid.

Limitations: False Trace results may occur with highly pigmented urine

specimens or those containing large amounts of levodopa metabolites. Compounds such as mesna (2-mercaptoethane sulfonic acid) that contain sulfhydryl groups may cause false positive results, or an atypical color reaction.

pH [pH]:

Expected values: The normal pH of urine can range from 4.6 to 8.0. Certain dietary conditions can produce acid or alkaline urines, which can be useful in the treatment of some calculi.[1]

Performance characteristics: The pH test area measures pH values from 5–8.5 visually and 5–9 instrumentally, generally to within one unit of the expected result. pH readings are not affected by variations in the urinary buffer concentration.

Limitations: Bacterial growth by certain organisms in a specimen may cause a marked alkaline shift (pH > 8.0), usually because of urea conversion to ammonia.

SPECIFIC GRAVITY [SG]:

Expected values: The normal SG of urine ranges from 1.001–1.035. If the specific gravity of a random urine is 1.023 or greater, the concentrating ability of the kidneys can be considered normal.[1]

Performance characteristics: This test permits determination of urine specific gravity between 1.000 and 1.030. In general, it correlates within 0.005 with values obtained with the refractive index method. For increased accuracy, 0.005 may be added to readings from urines with pH ≥ 6.5. Strips read instrumentally are automatically adjusted for pH by the instrument. The Siemens SG test is not affected by the presence of radiopaque dyes as are the refractive index, urinometer, and osmolality methods.

Limitations: The Siemens SG test is dependent on ions in urine and results may differ from those obtained with other specific gravity methods when certain nonionic urine constituents, such as glucose, are present. Highly buffered alkaline urines may cause low readings, while the presence of moderate quantities of protein (100–750 mg/dL) may cause elevated readings.

BILIRUBIN [BIL]:

Expected values: Normal adult urine contains about 0.02 mg/dL of bilirubin, which is not detectable by even the most sensitive methods. Even trace amounts of bilirubin are sufficiently abnormal to require further investigation.[1] Since very small amounts of bilirubin (0.1 mg/dL or greater) may be found in the earliest phases of liver disease, the user must consider whether the sensitivity of Siemens Reagent Strips to bilirubin is sufficient for the intended use. When very small amounts of bilirubin in urine are sought (e.g., in the earliest phase of viral hepatitis), ICTOTEST® Reagent Tablets should be the method of choice.

Sensitivity: 0.4–0.8 mg/dL bilirubin

Performance characteristics: The test is specific for bilirubin and will not react with any other substance normally excreted in urine.

Limitations: Indican (indoxyl sulfate) can produce a yellow-orange to red color response that may interfere with the interpretation of a negative or positive reading. Metabolites of Lodine® (etodolac) may cause false positive or atypical results. Atypical colors (colors that are unlike the negative or positive color blocks shown on the Color Chart) may indicate that bilirubin-derived bile pigments are present in the urine sample and may be masking the bilirubin reaction. These colors may indicate bile pigment abnormalities and the urine specimen should be tested further (e.g., ICTOTEST Reagent Tablets).

UROBILINOGEN [URO]:

Expected values: Urobilinogen is normally present in urine at concentrations up to 1.0 mg/dL (1 Ehrlich Unit/dL). A result of 2.0 mg/dL represents the transition from normal to abnormal, and the patient and/or urine specimen should be evaluated further for hemolytic and hepatic disease. Evaluation of both the bilirubin and urobilinogen results helps in the differential diagnosis of jaundice, as well as other liver and biliary disorders.[1]

Performance characteristics: This test area will detect urobilinogen in concentrations as low as 0.2 mg/dL (0.2 EU/dL) in urine. The absence of uroblinogen in the specimen cannot be determined.

Limitations: The test pad may react with interfering substances known to react with Ehrlich's reagent, such as p-aminosalicylic acid and sulfonamides. Atypical color reactions may be obtained in the presence of high concentrations of p-aminobenzoic acid. False negative results may be obtained if formalin is present. Strip reactivity increases with temperature; the optimum temperature is 22–26°C (72–79°F). The test is not a reliable method for the detection of porphobilinogen.

HELPFUL HINTS:

- Do not remove the strip from the bottle until immediately before it is to be used for testing. Replace the cap immediately and tightly after removing the reagent strip. Do not touch the test areas of the strip.
- Do not read any test pad after 2 minutes; color changes that occur after this time are of no diagnostic value.
- Discoloration or darkening of the test pads 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 negative and positive control materials; (3) retest with fresh product. If proper results are not obtained, consult your local Siemens representative, or contact the Customer Service Department for advice on testing technique and results.
- Contamination of the urine specimen with skin cleansers containing chlorhexidine may affect protein (and to a lesser extent specific gravity and bilirubin) test results. The user should determine whether the use of such skin cleansers is warranted.
- It is especially important to use fresh urine to obtain optimal results with the tests for bilirubin and urobilinogen, as these compounds are very unstable when exposed to room temperature and light.

CHEMICAL PRINCIPLES OF PROCEDURES AND INGREDIENTS:

(based on dry weight at time of impregnation)

Protein: This test is based on the protein-error-of-indicators principle. At a constant pH, the development of any green color is due to the presence of protein. Colors range from yellow for "Negative" through yellow-green and green to green-blue for "Positive" reactions. **Ingredients:** 0.3% w/w tetrabromphenol blue; 97.3% w/w buffer; 2.4% w/w nonreactive ingredients.

Blood: This test is based on the peroxidase-like activity of hemoglobin, which catalyzes the reaction of diisopropylbenzene dihydroperoxide and 3,3',5,5'-tetramethylbenzidine. The resulting color ranges from orange through green; very high levels of blood may cause the color development to continue to blue. **Ingredients:** 6.8% w/w diisopropylbenzene dihydroperoxide; 4.0% w/w 3,3',5,5'-tetramethylbenzidine; 48.0% w/w buffer; 41.2% w/w nonreactive ingredients.

Leukocytes: Granulocytic leukocytes contain esterases that catalyze the hydrolysis of the derivatized pyrrole amino acid ester to liberate 3-hydroxy-5-phenyl pyrrole. This pyrrole then reacts with a diazonium salt to produce a purple product. **Ingredients:** 0.4% w/w derivatized pyrrole amino acid ester; 0.2% w/w diazonium salt; 40.9% w/w buffer; 58.5% w/w nonreactive ingredients.

Nitrite: This test depends upon the conversion of nitrate (derived from the diet) to nitrite by the action of Gram-negative bacteria in the urine. At the acid pH of the reagent area, nitrite in the urine reacts with p-arsanilic acid to form a diazonium compound. This diazonium compound in turn couples with 1,2,3,4-tetrahydrobenzo(h)quinolin-3-ol to produce a pink color. **Ingredients:** 1.4% w/w p-arsanilic acid; 1.3% w/w 1,2,3,4-tetrahydrobenzo(h)quinolin-3-ol; 10.8% w/w buffer; 86.5% w/w nonreactive ingredients.

Glucose: This test is based on a double sequential enzyme reaction. One enzyme, glucose oxidase, catalyzes the formation of gluconic acid and hydrogen peroxide from the oxidation of glucose. A second enzyme, peroxidase, catalyzes the reaction of hydrogen peroxide with a potassium iodide chromogen to oxidize the chromogen to colors ranging from green to brown. **Ingredients:** 2.2% w/w glucose oxidase (microbial, 1.3 IU); 1.0% w/w peroxidase (horseradish, 3300 IU); 8.1% w/w potassium iodide; 69.8% w/w buffer; 18.9% w/w nonreactive ingredients.

Ketone: This test is based on the development of colors ranging from buff-pink, for a negative reading, to maroon when acetoacetic acid reacts with nitroprusside. **Ingredients:** 7.1% w/w sodium nitroprusside; 92.9% w/w buffer.

pH: This test is based on a double indicator principle that gives a broad range of colors covering the entire urinary pH range. Colors range from orange through yellow and green to blue. **Ingredients:** 0.2% w/w methyl red; 2.8% w/w bromthymol blue; 97.0% w/w nonreactive ingredients.

Specific Gravity: This test is based on the apparent pKa change of certain pretreated polyelectrolytes in relation to ionic concentration. In the presence of an indicator, colors range from deep blue-green in urine of low ionic concentration through green and yellow-green in urines of increasing ionic concentration. **Ingredients:** 2.8% w/w bromthymol blue; 68.8% w/w poly (methyl vinyl ether/maleic anhydride); 28.4% w/w sodium hydroxide.

Bilirubin: This test is based on the coupling of bilirubin with diazotized dichloroaniline in a strongly acid medium. The color ranges through various shades of tan. **Ingredients:** 0.4% w/w 2,4-dichloroaniline diazonium salt; 37.3% w/w buffer; 62.3% w/w nonreactive ingredients.

Urobilinogen: This test is based on the Ehrlich reaction in which p-diethylaminobenzaldehyde in conjunction with a color enhancer reacts with urobilinogen in a strongly acid medium to produce a pink-red color. **Ingredients:** 0.2% w/w p-diethylaminobenzaldehyde; 99.8% w/w nonreactive ingredients.

AVAILABILITY: Siemens Reagent Strips for Urinalysis are available in bottles of 100 strips: MULTISTIX® 10 SG (#2161); MULTISTIX® 9 (#2162); MULTISTIX® 9 SG (#2163); MULTISTIX® 8 SG (#2164); MULTISTIX® 7 (#2165); MULTISTIX® (#2179); and LABSTIX® (#2181).

U.S. PATENT NUMBERS: Refer to the carton of the product you are using for applicable patent numbers.

TRADEMARKS:

Refer to the carton of the product you are using for the applicable Siemens trademarks.

Azo Gantrisin and Azo Gantanol are trademarks of Hoffman-La Roche, Inc.

Capoten is a trademark of Par Pharmaceutical, Inc.

Furadantin is a trademark of Shionogi Pharma.

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Lodine is a trademark of Victory Pharma, Inc.

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TECHNICAL ASSISTANCE:

For technical support, contact your local technical support provider or distributor.

In the US call 877-229-3711.

www.siemens.com/diagnostics

P-5318-J

Status Strep A

Direct Group A Streptococcus Antigen Test

For Professional *In Vitro* Use

Immunoassay for the qualitative detection of group A streptococcal antigen directly from throat swab specimens

LifeSign, LLC

CLIA Complexity:	Waived
CDC Analyte Identifier Code:	5810

Item No. 34130 30 Test Kit

Intended Use

Status Strep A—Direct Group A Streptococcus Antigen Test Strip is a rapid immunochromatographic assay for the qualitative detection of group A streptococcal antigen directly from throat swab specimens. The test is intended for use in the physician's offices, hospitals, and clinical laboratories as an aid in the clinical diagnosis of group A streptococcal infection[1].

Summary and Explanation

Group A streptococcus is one of the most significant human pathogens causing acute pharyngitis, tonsillitis, impetigo, and scarlet fever [1]. It is very important to differentiate streptococcal infection from other etiologic agents (e.g., viral, mycoplasmal, or chlamydial) so that appropriate therapy may be initiated. Classical methods for identification require 18–48 hours culture time for throat swab specimens or other exudates to produce results showing bacitracin susceptible beta-hemolytic streptococci. Rapid diagnosis and timely treatment of group A streptococcal pharyngitis infections will reduce the severity of symptoms and further complications such as rheumatic fever and glomerulonephritis [2-6].

Principle

Status Strep A is a rapid immunochromatographic assay for the qualitative detection of group A streptococcal antigen directly from throat swabs. The ***Status Strep A*** test involves the chemical extraction of group A streptococcal antigen followed by solid-phase immunoassay technology for the detection of extracted antigen. In the test procedure, a throat swab specimen is collected, placed into a mixture of Reagent A and B, and extracted for 1–2 minutes. The ***Status Strep A*** strip is then inserted into the tube containing the extract and the extract is allowed to migrate up the test strip. If group A streptococci are present in the specimen, they will react with the conjugate dye and then react with the antibody in the Test line, to generate a colored Test line. The rest of the sample and dye continues to migrate to the control area, where antibody to the strep A antibody is immobilized. In this area, the conjugate of anti-Strep A antibody and red dye react with anti-rabbit IgG antibody, to generate a red line. Presence of two colored lines, one Test line and one Control line, indicates a positive result, while the absence of a Test line in the reading area indicates a negative result. In the absence of antigen in the sample, only the control line will develop.

The control line provides an additional quality control since it will only appear if:

1. The anti-strep A antibody on the colloidal gold is active.
2. The proper amount of sample is used.
3. The wicking chemistry is working properly.

In the absence of the control line, the test should be considered invalid and should be repeated with a new strip and a new swab sample.

Reagents and Materials Provided

- Each ***Status Strep A*** test kit contains all necessary reagents and materials for 30 tests.
- ***Status Strep A*** test strip: Contains a membrane coated with rabbit antigroup A streptococcus antibody for the test line and a second control antibody, and a conjugate pad impregnated with the rabbit anti-strep A antibody-dye complex.
- Extraction Reagent A (6.5 mL): 2.0 M sodium nitrite solution. (Warning: Avoid contact with eyes or skin.)
- Extraction Reagent B (6.5 mL): 0.2 M phosphoric acid solution. (Warning: Avoid contact with eyes or skin.)
- Positive Control (1 mL): Extracted (non-infective) group A streptococcus antigen (equivalent to approximately 1 X 10^7 CFU/ml) in phosphate buffered saline containg 0.1% sodium azide.
- Negative Control (1 mL): Extracted (non-infective) group B streptococcus antigen in phosphate buffered saline containg 0.1% sodium azide.
- Extraction Tubes (30)
- Throat Swabs (30): Rayon swab with plastic shaft (use only the swabs supplied).
- Instructions for Use

Materials Required but Not Provided

- Timer
- Reagent tube rack

Warning and Precautions

- For in vitro diagnostic use only.
- Do not interchange materials from different product lots.
- Do not use after the expiration date indicated.
- The test kit should be used only with the swabs supplied with the kit.
- Do not interchange caps between reagents.
- Reagents A and B are slightly caustic. Avoid contact with eyes, sensitive mucous membranes, cuts, abrasions, etc. If these reagents come in contact with the skin or eyes, flush with a large volume of water.
- Do not smoke, eat or drink in areas where the specimens or kit reagents are handled.
- Wear disposable gloves while handling the kit reagents or specimens and wash hands thoroughly afterwards.
- All patient samples should be handled as if capable of transmitting disease. Observe established precautions against microbiological hazards throughout all procedures and follow standard procedures for proper disposal of specimens.
- The ***Status Strep A*** test strip should remain in its original sealed pouch until ready for use. Do not use if the pouch is damaged or the seal is broken.
- The control solutions contain sodium azide, which, on contact with lead or copper plumbing, may react to form explosive metal azides. Use a large volume of water to flush reagents on disposal.

Storage and Stability

Status Strep A test strip should be stored at 2–30°C (35–86°F) in its original sealed pouch, out of direct sunlight. Do not freeze. Kit contents are stable until the expiration date printed on the outer box.

Specimen Collection and Preparation

Collect throat swab specimens following standard clinical procedures, using the sterile rayon swabs supplied with this kit. Throat swab specimens should be collected by health care professionals only.

- Collect throat swab specimens following standard clinical procedures using the swabs supplied in this kit.
- Swabs should be processed within 4 hours after collection, unless they are stored in a refrigerator (2–8°C). If stored in a refrigerator, swab should be processed within 24 hours from collection.
- If a culture is required, it is recommended that two swab samples be collected. The first swab sample should be used for testing with ***Status Strep A*** as soon as possible after collection. The second swab may be stored in a liquid medium (about 200 µL) such as a Modified Stuart's or equivalent, for up to 24 hours in the refrigerator.
- Care should be taken in collecting the throat swab specimens to avoid touching sides of the mouth while sampling inflamed or exudative areas. Presence of excess amount of saliva or blood in the collected sample would interfere with test results.

Procedure

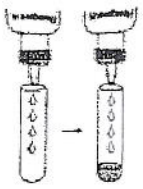
Procedural notes

These instructions must be followed carefully to achieve optimal test results. Follow the assay procedure and always perform the test under carefully standardized conditions.

- If specimens, kit reagents or ***Status Strep A*** have been stored in the refrigerator, allow them to reach room temperature before use.
- Do not open the foil pouch until you are ready to perform the test.
- Several tests may be run at one time.
- To avoid contamination of reagents, do not allow the tips of the reagent bottles to come in contact with the extraction tubes.
- To add Reagents A and B, hold the bottles in a vertical position above the extraction tube and dispense 4 drops each into the tube.
- Before adding the test strip to the reaction tube, remove the swab by squeezing the liquid from the swab (squeezing the flexible extraction tube), and insert the strip.
- Handle all specimens as if they are capable of transmitting disease.
- After testing, dispose of the ***Status Strep A***, throat swab, and extraction tube following proper laboratory practices. Consider any material that comes into contact with specimen as potentially infectious.

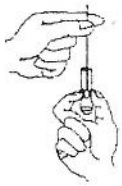
Test Protocol

1. Just before testing, add 4 drops of Reagent A (yellow) and 4 drops of Reagent B to the extraction tube. Mix solution by shaking the tube gently. (The solution should turn pink.)



2. Immediately put the swab into the tube.
3. Rotate the swab vigorously in the extraction solution to extract specimen thoroughly.

4. Let stand for 1–2 minutes
5. Squeeze out as much liquid as possible from the swab by pressing the swab firmly against the side of the tube with two fingers.

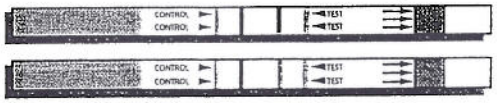


6. Discard the swab.
7. Take out the ***Status Strep A*** test strip from the sealed pouch.

8. Insert the ***Status Strep A*** test strip into the tube of extracted solution and allow the migration to begin.
9. Read the result in 5 minutes, after a distinct color line has formed in the reading window, but no later than 10 minutes after the test strip has been dipped in the extracted solution.

Interpretation of Results

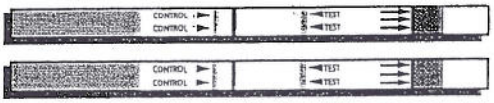
POSITIVE



Two reddish-purple colored lines, both a Control line and Test line, indicate that group A streptococcal antigen has been detected.

Note: The Test line may have a color shade of varying intensity depending on the concentration of antigen detected (weak to strong). The intensity of the Control line should not be compared to that of the Test line for the interpretation of the test result

NEGATIVE



Only one colored line in the Control line area, and no distinct colored line in the Test line area indicates that the specimen does not contain detectable levels of group A streptococcal antigen and is considered as presumptive negative. It is recommended by the American Academy of Pediatrics [7] that presumptive negative results be confirmed by culture.

INVALID

A distinct colored line in the Control line area (C) should always appear. The test is invalid if no Control line forms in 5 minutes. When the test shows an invalid result, the test should be repeated with a new test strip and a new swab sample.

Limitations

- As is the case with any other diagnostic procedure, the results obtained with this kit must be used only as an adjunct to other information available to the physician.
- This test should be used only for the qualitative detection of strep A antigen. Use of the kit for the semi-quantitative determination of group A strep has not been established.
- This test will not differentiate between a carrier and an infected individual.
- The ***Status Strep A*** test can detect non-viable as well as viable organisms. The test may therefore detect organisms which cannot be demonstrated in culture.

- This test is not intended as a substitute for bacterial culture testing; test results should be compared with culture identification until each laboratory establishes its own equivalences of performance. Additional follow-up testing using the culture method is recommended if the Status Strep A™ test result is negative and group A streptococcal infection is suspected.
- Test specimens heavily colonized with Staphylococcus aureus (> 10^{10} CFU/mL) can yield false positive results.
- Proper throat swabs must be obtained for good quality tests.
- Pharyngitis can be caused by organisms other than group A streptococcus. This test does not provide any further information about pharyngitis other than the possibility of strep A infection. If clinical signs and symptoms are not consistent with laboratory results, a follow-up throat culture and grouping procedure should be performed. Pharyngitis is also caused by other serological groups of streptococcus as well as other organisms.
- A negative result may be obtained due to poor sample collection, or at the onset of the disease due to a low antigen level, below the sensitivity limit of the test. If symptoms persist or intensify, repeat testing with a fresh sample is recommended. Test the fresh sample by culture method to confirm the negative test result obtained with ***Status Strep A*** [7].
- Swabs transported in liquid media prior to testing may result in reduced sensitivity due to dilution of organisms.

Quality Control

External Quality Control:

- Good laboratory practice recommends the use of external positive and negative controls to assure the test reagents are working properly and that the user has performed test correctly. If the controls do not perform as expected, review the instructions for use to see if the test was performed correctly and repeat the test or contact LifeSign Technical Assistance before performing patient specimens. The built-in purplish-red Control line indicates only the integrity of the test strip and proper fluid flow.
- It is recommended that the control test be performed, using the controls provided, before using a new lot or shipment of ***Status Strep A*** kits to confirm the expected Q.C. results. The frequency of additional Q.C. tests should be determined according to your laboratory's standard Q.C. procedures. Upon confirmation of the expected results, the kit is ready for use with patient specimens.
- The Negative control will yield a negative result (Control line only) when the test has been performed correctly and the test device is functioning properly. Add 4 drops each of Reagents A and B into an extraction tube, then add one drop of Negative Control and mix thoroughly. Process the extraction in the same manner as you would for a patient specimen according to the Test Procedure.
- The Positive control will produce a moderate positive result (two lines) when the test has been performed correctly and the test strip is functioning properly. Add 4 drops each of Reagents A and B into an extraction tube, then add one drop of Positive Control and mix thoroughly. Process the extraction in the same manner as you would for a patient specimen according to the Test Procedure.
- In addition to the external positive control provided with the kit, a known live culture of Streptococcus pyogenes (strep A) such as ATCC strain 19615 can be used for quality control testing. Live culture from an agar plate may be collected by swab and tested the same way as described for unknown samples in the Test Procedure. Negative control can be used to dilute the culture organism to make a Positive control.
- A known live culture of group C streptococci such as ATCC strain 12388 can be used for negative quality control testing at a minimum concentration of 10^6 inactivated CFU per mL. Process the extraction in the same manner as you would for a patient specimen according to the Test Procedure.
- The Positive and Negative controls provided with the kit do not monitor the extraction step. If the controls do not perform as expected, do not report patient results.
- The use of positive and negative controls from other commercial kits has not been established with ***Status Strep A.***

Internal Procedural Control:

- A colored line in the Control line area can be considered an internal positive procedural control. A distinct pinkish-purple control line will always appear if the test has been performed correctly. If the control line does not appear, the test is invalid and a new test should be performed. If the problem persists, contact LifeSign for technical assistance.
- A clear background in the result area is considered an internal negative procedural control. If the test is performed correctly and the test strip is working properly, the background in the result area should be clear, providing a distinct negative result.

Expected Values

Group A streptococcus infection exhibits a seasonal variation and is most prevalent in the winter and early spring. Approximately 19% of all upper respiratory tract infections are caused by group A streptococcus [7]. The highest incidence of this disease is found in high density populations, such as school aged children and military bases. Males and females are equally affected by the disease [8].

Performance Characteristics

Clinical Correlation:

The performance of the ***Status Strep A***— Direct Strep A Antigen Test was compared to that of BioSign™ Strep A test and the conventional plate culture techniques in a prospective evaluation of clinical specimens. Throat swab specimens were collected from 505 children and adult patients with pharyngitis symptoms.Each swab was first used to inoculate a sheep blood agar plate containing a bacitracin disk, and the swab was then assayed with ***Status Strep A*** to record ***Status Strep A*** test results. The plates were incubated at 37°C in 5% CO^2 for 18-24 hours to detect b-hemolytic colonies typical of group A streptococci. If the plates were negative, they were held for additional 18-24 hours. All samples were collected from cultured plates and assayed by a strep A confirmatory latex agglutination test (Streptex by Murex). All presumptive positive b-hemolytic colonies were serotyped by four other kinds of Streptex test kits (B, C, F, and G). Serotyping by five kinds of Streptex test kits (A, B, C, F, and G) was also performed when the borderline b-hemolytic results were obtained. These results constitute the confirmed 18/48 hour culture results.

The results are summarized below:

		Status Strep A (+)	(–)	Total
Confirmed (18/48 hour)	(+)	127	5	132
Culture Results	(–)	5	368	373
Total		132	373	505

Sensitivity (127/132): 96.2%
Specificity (368/373): 98.7%
Overall Accuracy (495/505): 98.0%

All of 373 specimens that were BioSign™ Strep A negative were also negative by ***Status Strep A*** for a relative specificity of 100%. All of 132 specimens that were BioSign™ Strep A positive were also positive by ***Status Strep A*** for a relative sensitivity of 100%. The overall agreement of both assay was 100%. The following table compares the sensitivity of the ***Status Strep A*** to the semi-quantitation of SBA culture.

SBA Culture Colony Count	No. of Positive: Hospital Culture	Confirmed	Status Strep A	% Sensitivity for Status Strep A
L (<20 colonies)	11	11	10*	90.9*
M (>20 and <50 colonies)	29	28	28	100
H (>50 colonies)	80	79	78**	98.7**
TOTAL	120	118	116	98.3*

* The lower sensitivity was probably due to the presence of culture plates with the colony count of less than 5.
** One high positive sample was found negative in the initial testing of the swab. However, testing the colony collected from the plate by ***Status Strep A*** confirm the positive result. There might have been the operator error in the initial testing. However, this was not confirmed.
% sensitivity for ***Status Strep A*** was calculated using the confirmed culture result.

Analytical Sensitivity

The analytical sensitivity of the test is 1.5 x 10^5 CFU/mL. This was established by testing a known number of organisms, ATCC 14285 or ATCC 19615, using Todd Hewette Broth from BBL. The cultured organisms were serially diluted in culture medium and tested by ***Status Strep A*** and BioSign™ Strep A. The same dilutions were cultured overnight on sheep blood agar plates from BBL for cell enumeration in CFU/mL. The assay results are as follows:

Cell Number in CFU/mL	Status Strep A Results
6.0 x 10^5	++ (medium positive)
3.0 x 10^5	+ (low positive)
1.5 x 10^5	+ (low positive)
7.7 x 10^4	– (negative)
3.8 x 10^4	– (negative)

Cross-Reactivity

To confirm the specificity of ***Status Strep A***, organisms likely to be found in the respiratory tract, as listed below, were tested at 1 x 10^7 organisms per mL. The results were all negative. Each organism (1 x 10^7 CFU/mL) was also spiked to a positive strep A control (3 x 10^5 CFU/mL) to confirm that the test results are the same as expected.

Organism Tested	Status Strep A Test Results A*	B
Escherichia coli (ATCC 11775)	–	+
Klebsiella pneumoniae (ATCC 13883)	–	+
Pseudomonas aeruginosa (ATCC 10145)	–	+
Candida albicans (ATCC 14053)	–	+
Neisseria gonorrhoeae (ATCC 9793)	–	+
Neisseria lactamica (ATCC 23970)	–	+
Neisseria meningitidis serogroup B (ATCC 13090)	–	+
Neisseria sicca (ATCC 9913)	–	+
Corynebacterium diphtheria (ATCC 296)	–	+
Proteus vulgaris (ATCC 6059)	–	+
Staphylococcus aureus Cowan (ATCC 12600)	–	+
Streptococcus pneumoniae (ATCC 6303)	–	+
Streptococcus Group B (ATCC 12386)	–	+
Streptococcus Group C (ATCC 12388)	–	+
Streptococcus Group D (ATCC 27284)	–	+
Streptococcus Group F, Type 2 (ATCC 12392)	–	+
Streptococcus Group G (ATCC 12394)	–	+
Staphylococcus epidermidis (ATCC 14990)	–	+
Haemophililus influenzae (ATCC 49401)	–	+
Branhamella catarrhalis (ATCC 25238)	–	+
Streptococcus sanguis (ATCC 10556)	–	+
Streptococcus mutans (ATCC 10449)	–	+
Negative Control	–	+
Positive Control	+	+

*A: 1 x 10^7 CFU/mL without strep A
B: 1 x 10^7 CFU/mL spiked with 3 x 10^5 CFU/mL strep A

Distribution of Random Error

Twenty blind samples prepared by spiking 4 different concentrations of group A streptococcal antigen, prepared from a known live culture of ATCC strain 19615, were separately tested by two operators. Five (5) replicate samples were prepared for each concentration: high positive samples containing approximately 4.8 x 10^6 CFU/mL medium positive samples containing approximately 1.2 x 10^6 CFU/mL, low positive samples containing approximately 3 x 10^5 CFU/mL, and negative samples. The test results from the two operators showed complete agreement.

Reproducibility Study

Reproducibility of ***Status Strep A*** test results was examined at two POL (physician's office laboratory) sites and a clinical laboratory, using a total of 15 blind control samples for total 90 tests. The panel consisted of 5 negative samples, 5 low positive samples containing approximately 3 x 10^5 CFU/mL, and 5 medium positive samples with approximately 1.2 x 10^6 CFU/ mL, prepared from a known live culture of ATCC strain 19615. The results obtained at each site agreed 100% with the expected results.

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Symbols Key

Instructions For Use (Read)		PRO	Procedure Card
REF	Catalog Number		Do Not Reuse
	Store At	IVD	For In Vitro Diagnostic Use
	Expiration Date	LOT	Lot Number
CONT	Contents		Manufacturer
SWAB	Throat Swab	MF	Manufactured for
DEV	Test Device	EC REP	Authorized Representative
IFU	Instructions For Use	CE	CE Mark

Printed in U.S.A.
P-5318-J
35-10/20/11

CE

EC REP
MT Promedt Consulting GmbH
Altenhofstrasse 80
66386 St. Ingbert
Germany
+49-68 94-58 10 20

Manufactured by PBM
Princeton BioMeditech Corporation
4242 U.S. Hwy 1, Monmouth Jct.
New Jersey 08852, U.S.A.
1-732-274-1000 www.pbmc.com

MF Manufactured for:
lifeSign
A PBM Group Company
85 Orchard Road,
Skillman, NJ 08558
800-526-2125, 732-246-3366
www.lifesignmed.com

Made in China 03/14

DN: 1155958103

CONSULT®

hCG Dipstick

A rapid, one step test for the qualitative detection of human chorionic gonadotropin (hCG) in urine. For professional *in vitro* diagnostic use only.

CLIA Category: Waived

INTENDED USE

The Consult® Diagnostics hCG Dipstick is a rapid chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine to aid in the early detection of pregnancy.

SUMMARY

Human chorionic gonadotropin (hCG) is a glycoprotein hormone produced by the developing placenta shortly after fertilization. In normal pregnancy, hCG can be detected in both urine and serum as early as 7 to 10 days after conception.[1,2,3,4] hCG levels continue to rise very rapidly, frequently exceeding 100 mIU/mL by the first missed menstrual period,[2,3,4] and peaking in the 100,000-200,000 mIU/mL range about 10-12 weeks into pregnancy. The appearance of hCG in both urine and serum soon after conception, and its subsequent rapid rise in concentration during early gestational growth, make it an excellent marker for the early detection of pregnancy.

The Consult® Diagnostics hCG Dipstick is a rapid test that qualitatively detects the presence of hCG in urine at the sensitivity of 25 mIU/mL. The test utilizes a combination of monoclonal and polyclonal antibodies to selectively detect elevated levels of hCG in urine. At the level of claimed sensitivity, the Consult® Diagnostics hCG Dipstick shows no cross-reactivity interference from the structurally related glycoprotein hormones hFSH, hLH and hTSH at high physiological levels.

PRINCIPLE

The Consult® Diagnostics hCG Dipstick is a rapid chromatographic immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in urine to aid in the early detection of pregnancy. The test utilizes a combination of antibodies including mouse monoclonal anti-hCG antibodies and goat polyclonal anti-hCG antibodies to selectively detect elevated levels of hCG. The assay is conducted by immersing the test dipstick in a urine specimen and observing the formation of colored lines. The specimen migrates via capillary action along the membrane to react with the colored conjugate.

Positive specimens react with the specific colored antibody conjugates and form a colored line at the test line region of the membrane. Absence of this colored line suggests a negative result. To serve as a procedural control, a colored line will always appear at the control line region if the test has been performed properly.

REAGENTS

The test dipstick contains mouse anti-beta hCG antibody conjugated to colloidal gold and goat anti-alpha hCG antibody coated on the membrane.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after the expiration date.
- The test dipstick should remain in the sealed pouch until use.
- All specimens should be considered potentially hazardous and handled in the same manner as an infectious agent.
- The test dipstick should be discarded in a proper biohazard container after testing.

STORAGE AND STABILITY

Store as packaged in the sealed pouch at 36-86°F/2-30°C. The test dipstick is stable through the expiration date printed on the sealed pouch. The test dipstick must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

SPECIMEN COLLECTION AND PREPARATION

A urine specimen must be collected in a clean and dry container. A first morning urine specimen is preferred since it generally contains the highest concentration of hCG; however, urine specimens collected at any time of the day may be used. Urine specimens exhibiting visible precipitates should be centrifuged, filtered, or allowed to settle to obtain a clear specimen for testing.

SPECIMEN STORAGE

Urine specimens may be stored at 36-46°F/2-8°C for up to 48 hours prior to testing. For prolonged storage, specimens may be frozen and stored below -4°F/-20°C. Frozen specimens should be thawed and mixed before testing.

MATERIALS

MATERIALS PROVIDED

- Test dipsticks
- Package insert
- Procedure card

MATERIALS REQUIRED BUT NOT PROVIDED

- Specimen collection container
- Timer

DIRECTIONS FOR USE

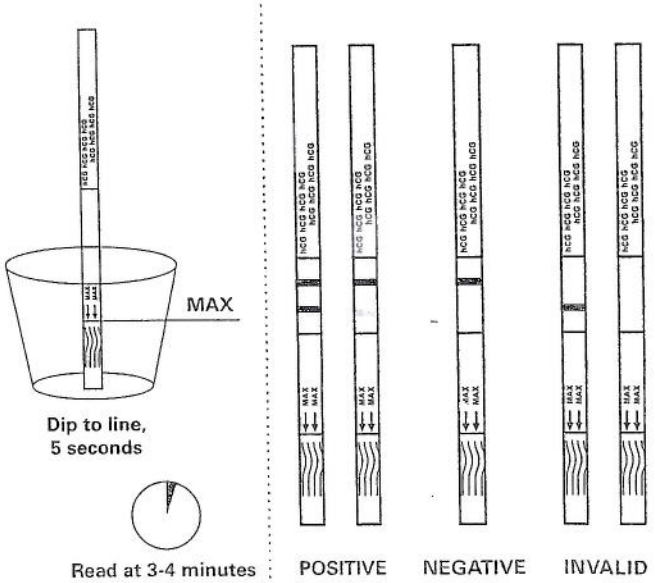
Allow the test dipstick, urine specimen and/or controls to equilibrate to room temperature (59-86°F/15-30°C) prior to testing.

1. Remove the test dipstick from the sealed pouch and use it as soon as possible.
2. With arrows pointing toward the urine specimen, immerse the test dipstick vertically in the urine specimen for at least 5 seconds. Do not pass the maximum line (MAX) on the test dipstick when immersing the dipstick (refer to illustration).
3. Place the test dipstick on a non-absorbent, flat surface, start the timer and wait for the red line(s) to appear. **Read the result at 3-4 minutes. Do not interpret results after the appropriate read time.** It is important that the background is clear before the result is read.

INTERPRETATION OF RESULTS

(Please refer to the illustration above)

POSITIVE*: Two distinct red lines appear. One line should be in the control region (C) and another line should be in the test region (T).



Note: A sample hCG concentration below the cut-off level of this test might result in a weak line appearing in the test region (T) after an extended period of time. A line in the test region (T) seen after the read time could be indicative of a low hCG level in the sample. If such results are seen, it is recommended that the test be repeated with a new sample in 48-72 hours or that an alternate confirmation method is used.

NEGATIVE: One red line appears in the control region (C). No apparent red or pink line appears in the test region (T).

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test dipstick. If the problem persists, discontinue using the test kit immediately and contact Technical Support at (866) 216-0094.

*Note: The intensity of the red color in the test line region (T) will vary depending on the concentration of hCG present in the specimen. However, neither the quantitative value nor the rate of increase in hCG can be determined by this qualitative test.

QUALITY CONTROL

Internal procedural controls are included in the test. A red line appearing in the control region (C) is the internal procedural control. It confirms sufficient specimen volume and correct procedural technique. A clear background is an internal negative background control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

It is recommended that a positive hCG control (containing ≥ 25 mIU/mL hCG in urine) and a negative hCG control (containing "0" mIU/mL hCG) be evaluated to verify proper test performance with each new lot, each new shipment, monthly as a check on storage, each new untrained operator and as otherwise required by your lab internal quality system procedures.

LIMITATIONS

1. Very dilute urine specimens, as indicated by a low specific gravity, may not contain representative levels of hCG. If pregnancy is still suspected, a first morning urine specimen should be collected 48 hours later and tested.
2. False negative results may occur when the levels of hCG are below the sensitivity level of the test. When pregnancy is still suspected, a first morning urine specimen should be collected 48 hours later and tested.
3. Very low levels of hCG (less than 50 mIU/mL) are present in urine specimen shortly after implantation. However, because a significant number of first trimester pregnancies terminate for natural reasons,[5] a test result that is weakly positive should be confirmed by retesting with a first morning urine specimen collected 48 hours later.
4. This test reliably detects intact hCG up to 500,000 mIU/mL. It does not reliably detect hCG degradation products, including free-beta hCG and beta core fragments. Quantitative assays used to detect hCG may detect hCG degradation products and therefore may disagree with the results of this rapid test.
5. A number of conditions other than pregnancy, including trophoblastic disease and certain non-trophoblastic neoplasms including testicular tumors, prostate cancer, breast cancer, and lung cancer, cause elevated levels of hCG.[6,7] Therefore, the presence of hCG in urine specimen should not be used to diagnose pregnancy unless these conditions have been ruled out.
6. This test provides a presumptive diagnosis for pregnancy. A confirmed pregnancy diagnosis should only be made by a physician after all clinical and laboratory findings have been evaluated.

EXPECTED VALUES

Negative results are expected in healthy non-pregnant women and healthy men. Healthy pregnant women have hCG present in their urine and serum specimens. The amount of hCG will vary greatly with gestational age and between individuals.

The Consult® Diagnostics hCG Dipstick has a sensitivity of 25 mIU/mL, and is capable of detecting pregnancy as early as 1 day after the first missed menses.

PERFORMANCE CHARACTERISTICS

ACCURACY

A multi-center clinical evaluation was conducted comparing the results obtained using the Consult® Diagnostics hCG Dipstick to another commercially available urine membrane hCG test. The study included 150 urine specimens: both assays identified 72 negative and 78 positive results. The results demonstrated 100% overall agreement (for an accuracy of > 99%) of the Consult® Diagnostics hCG Dipstick when compared to the other urine membrane hCG test.

		Reference hCG Method	
		Positive	Negative
Consult® Method	Positive	78	0
	Negative	0	72

SENSITIVITY AND SPECIFICITY

The Consult® Diagnostics hCG Dipstick detects hCG at a concentration of 25 mIU/mL or greater. The test has been standardized to the W.H.O. Third International Standard. The addition of LH (300 mIU/mL), FSH (1,000 mIU/mL), and TSH (1,000 µIU/mL) to negative (0 mIU/mL hCG) and positive (25 mIU/mL hCG) specimens showed no cross-reactivity.

INTERFERING SUBSTANCES

The following potentially interfering substances were added to hCG negative and positive specimens.

All substances listed in mg/dL unless otherwise noted.

Acetaminophen	20	Acetone	1,000
Acetylsalicylic Acid	20	Acetoacetic Acid	2,000
Ampicillin	20	Ascorbic Acid	20
Atropine	20	Albumin	2,000
ß-Hydroxybutyrate salt	2,000	Benzoylecgonine	10
Bilirubin	20	Brompheniramine	20
Caffeine	20	Cannabinol	10
Clomiphene	100	Cocaine	10
Codeine	10	Cholesterol	500
Creatine	20	Dextromethorphan	20
DMSO	5%	EDTA	80
Ephedrine	20	Ethanol	1%
Estriol	2	Estrone 3-Sulfate	10
Gentisic Acid	20	Glucose	2,000
Hemoglobin	1,000	Heroin	1
Ibuprofen	20	Methadone	10
Methamphetamine	10	Methanol	10%
Morphine	0.6	Oxalic Acid	40
Phenothiazine	20	Phenylpropanolamine	20
Pregnanediol	2	Salicylic Acid	20
Tetracycline	20	Triglycerides	1,200
Theophylline	20	Urea	2,000
Uric Acid	20		

None of the substances at the concentration tested interfered in the assay.

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Manufactured for PSS World Medical, Inc.
4345 Southpoint Blvd., Jacksonville, FL 32216

Made in China 07/16

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Clearview® MONO Whole Blood

A rapid test for the qualitative detection of Infectious Mononucleosis (IM) heterophile antibodies in whole blood. For professional *in vitro* diagnostic use only. Rx Only.

CLIA Category: Waived

INTENDED USE

The Clearview® MONO test (Whole Blood) is a rapid chromatographic immunoassay for the qualitative detection of Infectious Mononucleosis heterophile antibodies in whole blood to aid in the diagnosis of infectious Mononucleosis.

SUMMARY

Infectious Mononucleosis is caused by the Epstein-Barr virus, which is a member of the herpesvirus family. Symptoms of IM are fever, sore throat and swollen lymph glands. In very rare cases, heart or central nervous system problems may occur. Diagnosis of IM is made based on the presence of heterophile antibodies. Infectious mononucleosis heterophile antibodies belong to the IgM class. They are present in 80-90% of acute IM cases and can be detected in 60-70% of patients during the first week of clinical illness.[1-4]

The Clearview MONO test (Whole Blood) is a simple test that utilizes an extract of bovine erythrocytes to qualitatively and selectively detect IM heterophile antibodies in whole blood in just minutes.

PRINCIPLE

The Clearview MONO test (Whole Blood) is a qualitative membrane strip based immunoassay for the detection of IM heterophile antibodies in whole blood. In this test procedure, bovine erythrocyte extracted antigen is coated on the test line region of the cassette. The sample reacts with bovine erythrocyte extracted antigen coated particles that have been applied to the label pad. This mixture migrates chromatographically along the length of the test strip and interacts with the coated bovine erythrocyte extracted antigen. If the sample contains IM antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain IM heterophile antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

The test cassette contains bovine erythrocyte extracted antigen-coated particles and bovine erythrocyte extracted antigen coated membrane.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.
- Do not eat, drink or smoke in the area where the specimen samples and kits are handled.
- The negative control contains human plasma. Handle controls and all specimen samples as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimen samples.
- The positive and negative controls contain sodium azide as a preservative, which may form potentially explosive metal azide if it reacts with lead or copper plumbing. Large quantities of water should be used to flush discarded controls down a sink.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimen samples are assayed.
- Humidity and temperature can adversely affect results.

STORAGE AND STABILITY

The kit can be stored at room temperature or refrigerated (2-30°C). The test cassette is stable through the expiration date printed on the sealed pouch. The test cassette must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

SAMPLE COLLECTION AND PREPARATION

The Clearview MONO test (Whole Blood) can be performed using whole blood from venipuncture or fingerstick.

To collect Venipuncture Whole Blood samples:
Collect anti-coagulated blood sample (sodium or potassium heparin, sodium or potassium EDTA, sodium or potassium citrate and sodium oxalate) following standard laboratory procedures.

To collect Fingerstick Whole Blood samples:

- Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
- Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
- Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
- Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
- Holding the capillary tube horizontally, touch the end of the tube to the blood until filled to the line; avoid air bubbles.
- Place the bulb onto the top end of the capillary tube.
- Squeeze the bulb to dispense the whole blood.

Testing should ideally be performed immediately after the samples have been collected. Do not leave the samples at room temperature for prolonged periods. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Whole blood collected by fingerstick should be tested immediately. Do not freeze whole blood samples.

If samples are to be shipped, they should be packed in compliance with federal regulations covering the transportation of etiologic agents.

MATERIALS

MATERIALS PROVIDED

- 30 Test cassettes
- 30 Disposable pipettes
- 40 Disposable heparinized capillary tubes and 2 dispensing bulbs
- 1 Positive control (1 mL; Goat anti-mono antibody, 0.09% sodium azide)
- 1 Negative control (1 mL; Diluted human plasma, 0.09% sodium azide, infection risk)
- 1 Sample buffer (5 mL; Disodium hydrogen phosphate, sodium chloride and casein, 0.09% sodium azide)
- 1 Directional insert

MATERIALS REQUIRED BUT NOT PROVIDED

- Sample collection container (for venipuncture whole blood)
- Lancet (for fingerstick whole blood only)
- Timer

DIRECTIONS FOR USE

(Please refer to the illustration)
Allow the test cassette, sample, buffer and controls to reach to room temperature (15-30°C) before testing.

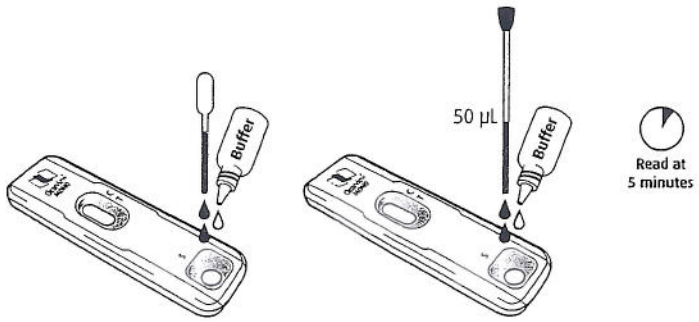
1. Remove the test cassette from the foil pouch and use it as soon as possible. For best results, perform the test immediately after opening the foil pouch.

2. Place the test cassette on a clean and level surface.

   For **Whole Blood (Venipuncture)** samples: Hold the pipette upright and add **2 drops of whole blood** (about 50 µL) to the sample well (S) of the test cassette. Then add **1 drop of Sample Buffer** to the sample well (S). Start the timer.

   For **Whole Blood (Fingerstick)** samples: Add **one capillary tube of blood** (about 50 µL) to the sample well (S) of the test cassette. Then add **1 drop of Sample Buffer** to the sample well (S). Start the timer.

3. Wait for the red line(s) to appear. The result should be read at 5 minutes. The background should be clear before the result is read. Do not read the result after 10 minutes.



2 drops of **Venipuncture** whole blood + 1 drop of Buffer **OR** 50 µL **Fingerstick** whole blood + 1 drop of Buffer

INTERPRETATION OF RESULT

POSITIVE **NEGATIVE** **INVALID**

POSITIVE*: Two distinct red lines appear. One line should be in the control line region (C) and another line should be in the test line region (T). A positive result means that IM heterophile antibodies were detected in the sample.
*NOTE: The shade of the red color in the test line region (T) will vary based on the amount of IM heterophile antibodies in the sample. Any shade of red in the test line region (T) should be considered positive.

NEGATIVE: One red line appears in the control line region (C). No apparent red or pink line appears in the test line region (T). A negative result means that IM heterophile antibodies were not found in the sample or are below the detection limit of the test.

INVALID: No line appears in the control line region (C). If this occurs, read the directions again and repeat the test with a new test cassette. If the result is still invalid, stop using the test kit and contact Alere Technical Support at (866) 216-0094.

QUALITY CONTROL

INTERNAL QUALITY CONTROL

Internal procedural controls are included in the test. A red line appearing in the control region (C) is an internal positive procedural control. It confirms sufficient sample volume, adequate membrane wicking and correct procedural technique. A clear background is an internal negative background control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

EXTERNAL QUALITY CONTROL

Quality control requirements must be performed in accordance with local, state, and federal regulations or accreditation requirements. Optimally, Alere recommends that positive and negative external controls be run with each new lot and with each new untrained operator. External positive and negative controls are supplied in the kit. Other commercial controls are not recommended if they have not been validated with this product.

PROCEDURE FOR EXTERNAL QUALITY CONTROL TESTING

Using the positive or negative external controls in place of a patient sample, add 1 drop of positive or negative control solution to the sample well (S) of a new test cassette, then add 1 drop of Sample Buffer. Start the timer. Continue with Step 3 in the Directions For Use section.

If unexpected results are seen when running the controls, review the Directions for Use, Interpretation of Results and Limitations sections and repeat the test with another cassette. If the problem persists, discontinue use of the test kit immediately and contact Alere Technical Support at (866) 216-0094.

LIMITATIONS

1. The Clearview MONO test (Whole Blood) is for *in vitro* diagnostic use only. The test should be used for the detection of IM heterophile antibodies in whole blood samples only. Neither the quantitative value nor the rate of increase in Mononucleosis antibody concentration can be determined by this qualitative test.
2. The Clearview MONO test (Whole Blood) will only indicate the presence of IM heterophile antibodies in the sample and should not be used as the sole criteria for the diagnosis of Mononucleosis infection.
3. Grossly hemolysed samples will yield invalid results. Strictly follow the Directional Insert instructions to obtain accurate results.
4. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
5. This assay has not been established for patients under 18 years of age. A heterophile antibody response is observed in approximately 80-90% of adults and children with EBV-caused IM.[6]

EXPECTED VALUES

Epstein-Barr virus infection during adolescence or young adulthood causes infectious mononucleosis 35% to 50% of the time.[1,5]

The incidence of EBV-associated infectious mononucleosis in the USA has been estimated at 45 per 100,000 and is highest in adolescent and young adults- about 2 out of 1,000. No seasonal pattern of EBV infection exists. The incubation period is 10 to 60 days, though 7 to 14 days is common for children and adolescents.

PERFORMANCE CHARACTERISTICS

A total of 611 clinical samples were tested by three independent sites in a clinical study. Slide agglutination served as the reference method for the study. Serum, plasma and whole blood were also collected for the detection of IM heterophile antibodies by the Clearview MONO test.

Of the 611 clinical samples collected, 185 were considered positive and 426 clinical specimens were considered negative by slide agglutination method. The results for each sample matrix are summarized below.

SERUM

Clearview MONO	Slide agglutination +	Slide agglutination −
+	72	0
−	0	168

Positive Agreement = 72/72 > 99% (95%-100%)**
Negative Agreement = 168/168 > 99% (98%-100%)**

PLASMA

Clearview MONO	Slide agglutination +	Slide agglutination −
+	58	1
−	0	181

Positive Agreement = 58/58 > 99% (94%-100%)**
Negative Agreement = 181/182 > 99% (97%-99%)*

WHOLE BLOOD

Clearview MONO	Slide agglutination +	Slide agglutination −
+	50	0
−	5	76

Positive Agreement = 50/55 = 91% (80%-97%)*
Negative Agreement = 76/76 > 99% (95%-100%)**

ALL SPECIMENS

Clearview MONO	Slide agglutination +	Slide agglutination −
+	180	1
−	5	425

Positive Agreement = 180/185 = 97% (94%-99%)*
Negative Agreement = 425/426 > 99% (99%-99.99%)*
*Denotes 95% Confidence Interval
**Denotes 97.5% Confidence Interval

In addition, the clinical samples were tested with a commercially available rapid diagnostic test kit. 611 serum, plasma and whole blood specimens were used to compare the Clearview MONO test to a comparator test. The results showed a >99% agreement between the two test kits. The results for each sample matrix are summarized below.

SERUM

Clearview MONO	Comparator test +	Comparator test −
+	72	0
−	1	167

Positive Agreement= 72/73 = 99% (93%-99%)*
Negative Agreement= 167/167 > 99% (98%-100%)**

PLASMA

Clearview MONO	Comparator test +	Comparator test −
+	59	0
−	1	180

San Diego
Positive Agreement= 59/60 = 98% (91%-99%)*
Negative Agreement= 180/180 > 99% (98%-100%)**

WHOLE BLOOD

Clearview MONO	Comparator test +	Comparator test −
+	50	0
−	1	80

Positive Agreement= 50/51 = 98% (90%-99%)*
Negative Agreement= 80/80 > 99% (96%-100%)**

ALL SPECIMENS

Clearview MONO	Comparator test +	Comparator test −
+	181	0
−	3	427

Positive Agreement = 181/184 = 98% (95%-99%)*
Negative Agreement = 427/427 > 99% (99%-100%)**
*Denotes 95% Confidence Interval
**Denotes 97.5% Confidence Interval

INTERFERENCE STUDIES

No interference with the Clearview MONO test results was observed in samples containing high levels of hemoglobin (up to 10 mg/mL), bilirubin (up to 1,000 mg/dL) and human serum albumin (up to 100 mg/mL). The test results were also unaffected when the hematocrit was altered ranging from 20% to 60% and when icteric and lipemic samples were tested.

POL STUDIES

Three physicians' offices were used to conduct an evaluation of the Clearview MONO test. Personnel with various educational backgrounds performed the testing. Each physician's office tested a randomly coded panel of samples consisting of negative (15), low positive (15), moderate positive (15) and invalid (15) for three days. The results obtained had a >99% correlation with the expected results.

NON-LABORATORY USER STUDY

A total of 77 untrained, inexperienced, non-laboratory participants were enrolled at three separate locations to demonstrate that they could follow the product instructions and perform the Clearview MONO test (Whole Blood) and obtain results similar to those obtained by trained laboratory technicians. Each participant received four blinded spiked whole blood samples: one negative, one invalid, one low positive and one medium positive.

Study participants were instructed to follow the Directional Insert and Procedure instructions to test the provided samples and record their test results. No other instruction or training was given. Upon completion of the test, participants filled out a brief questionnaire regarding the test procedure and ease of use of the labeling. The following results were obtained:

Site	Low Positive	Medium Positive	Negative	Invalid	Total Correct
A	23/27=85% (66-96%)*	25/27=93% (76-99%)*	27/27>99% (87-100%)*	27/27>99% (87-100%)*	102/108=94% (88-98%)*
B	25/27=93% (76-99%)*	25/27=93% (76-99%)*	27/27>99% (87-100%)*	27/27>99% (87-100%)*	104/108=96% (91-99%)*
C	23/23>99% (85-100%)*	23/23>99% (85-100%)*	23/23>99% (85-100%)*	23/23>99% (85-100%)*	92/ 92>99% (96-100%)*

*Denotes 95% Confidence Interval

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San Diego, CA 92121 USA

Product No. 92401

Clearview® MONO Whole Blood, Serum, Plasma

A rapid test for the qualitative detection of Infectious Mononucleosis (IM) heterophile antibodies in whole blood, serum and plasma. For professional *in vitro* diagnostic use only. Rx Only.

	Whole blood	Serum, Plasma
CLIA Category:	Waived	Non-waived (moderate)

INTENDED USE

The Clearview® MONO test (Whole Blood/Serum/Plasma) is a rapid chromatographic immunoassay for the qualitative detection of Infectious Mononucleosis heterophile antibodies in whole blood, serum or plasma to aid in the diagnosis of infectious Mononucleosis.

SUMMARY

Infectious Mononucleosis is caused by the Epstein-Barr virus, which is a member of the herpesvirus family. Symptoms of IM are fever, sore throat and swollen lymph glands. In very rare cases, heart or central nervous system problems may occur. Diagnosis of IM is made based on the presence of heterophile antibodies. Infectious mononucleosis heterophile antibodies belong to the IgM class. They are present in 80-90% of acute IM cases and can be detected in 60-70% of patients during the first week of clinical illness.[1-4]

The Clearview MONO test is a simple test that utilizes an extract of bovine erythrocytes to qualitatively and selectively detect IM heterophile antibodies in whole blood, serum or plasma in just minutes.

PRINCIPLE

The Clearview MONO test is a qualitative membrane strip based immunoassay for the detection of IM heterophile antibodies in whole blood, serum or plasma. In this test procedure, bovine erythrocyte extracted antigen is coated on the test line region of the cassette. The sample reacts with bovine erythrocyte extracted antigen coated particles that have been applied to the label pad. This mixture migrates chromatographically along the length of the test strip and interacts with the coated bovine erythrocyte extracted antigen. If the sample contains IM antibodies, a colored line will appear in the test line region indicating a positive result. If the sample does not contain IM heterophile antibodies, a colored line will not appear in this region indicating a negative result. To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

The test cassette contains bovine erythrocyte extracted antigen-coated particles and bovine erythrocyte extracted antigen coated membrane.

PRECAUTIONS

- For professional *in vitro* diagnostic use only. Do not use after expiration date.
- Do not eat, drink or smoke in the area where the specimen samples and kits are handled.
- The negative control contains human plasma. Handle controls and all specimen samples as if they contain infectious agents. Observe established precautions against microbiological hazards throughout all procedures and follow the standard procedures for proper disposal of specimen samples.
- The positive and negative controls contain sodium azide as a preservative, which may form potentially explosive metal azide if it reacts with lead or copper plumbing. Large quantities of water should be used to flush discarded controls down a sink.
- Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimen samples are assayed.
- Humidity and temperature can adversely affect results.

STORAGE AND STABILITY

The kit can be stored at room temperature or refrigerated (2-30°C). The test cassette is stable through the expiration date printed on the sealed pouch. The test cassette must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

SAMPLE COLLECTION AND PREPARATION

The Clearview MONO test can be performed using whole blood (from venipuncture or fingerstick), serum or plasma.

To collect Venipuncture Whole Blood samples:
Collect anti-coagulated blood sample (sodium or potassium heparin, sodium or potassium EDTA, sodium or potassium citrate and sodium oxalate) following standard laboratory procedures.

To collect Fingerstick Whole Blood samples:

- Wash the patient's hand with soap and warm water or clean with an alcohol swab. Allow to dry.
- Massage the hand without touching the puncture site by rubbing down the hand towards the fingertip of the middle or ring finger.
- Puncture the skin with a sterile lancet. Wipe away the first sign of blood.
- Gently rub the hand from wrist to palm to finger to form a rounded drop of blood over the puncture site.
- Holding the capillary tube horizontally, touch the end of the tube to the blood until filled to the line; avoid air bubbles.
- Place the bulb onto the top end of the capillary tube.
- Squeeze the bulb to dispense the whole blood.

Separate serum or plasma from blood as soon as possible to avoid hemolysis. Use only clear, non-hemolyzed samples.

Testing should ideally be performed immediately after the samples have been collected. Do not leave the samples at room temperature for prolonged periods. Whole blood collected by venipuncture should be stored at 2-8°C if the test is to be run within 2 days of collection. Whole blood collected by fingerstick should be tested immediately. Do not freeze whole blood samples. Serum or plasma samples may be stored at 2-8°C for up to 3 days. For long term storage, samples should be kept below -20°C.

Bring samples to room temperature prior to testing. Frozen samples must be completely thawed and mixed well prior to testing. Samples should not be frozen and thawed repeatedly.

If samples are to be shipped, they should be packed in compliance with federal regulations covering the transportation of etiologic agents.

MATERIALS

MATERIALS PROVIDED

- 30 Test cassettes
- 30 Disposable pipettes
- 40 Disposable heparinized capillary tubes and 2 dispensing bulbs
- 1 Positive control (1 mL; Goat anti-mono antibody, 0.09% sodium azide)
- 1 Negative control (1 mL; Diluted human plasma, 0.09% sodium azide, infection risk)
- 1 Sample buffer (5 mL; Disodium hydrogen phosphate, sodium chloride and casein, 0.09% sodium azide)
- 1 Directional insert

MATERIALS REQUIRED BUT NOT PROVIDED

- Sample collection container (for venipuncture whole blood)
- Lancet (for fingerstick whole blood only)
- Centrifuge (for serum or plasma only)
- Timer

DIRECTIONS FOR USE

(Please refer to the illustration)
Allow the test cassette, sample, buffer and controls to reach to room temperature (15-30°C) before testing.

1. Remove the test cassette from the foil pouch and use it as soon as possible. For best results, perform the test immediately after opening the foil pouch.

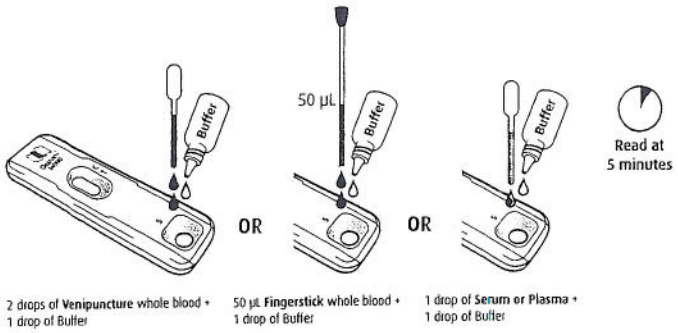
2. Place the test cassette on a clean and level surface.

   For **Whole Blood (Venipuncture)** samples: Hold the pipette upright and add **2 drops of whole blood** (about 50 µL) to the sample well (S) of the test cassette. Then add **1 drop of Sample Buffer** to the sample well (S). Start the timer.

   For **Whole Blood (Fingerstick)** samples: Add **one capillary tube of blood** (about 50 µL) to the sample well (S) of the test cassette. Then add **1 drop of Sample Buffer** to the sample well (S). Start the timer.

   For **Serum or Plasma** samples: Hold the pipette upright and add **1 drop of serum or plasma** (about 25 µL) to the sample well (S) of the test cassette. Then add **1 drop of Sample Buffer** to the sample well (S). Start the timer. Avoid trapping air bubbles in the sample well (S). See the illustration above.

3. Wait for the red line(s) to appear. The result should be read at 5 minutes. The background should be clear before the result is read. Do not read the result after 10 minutes.



INTERPRETATION OF RESULT

POSITIVE*: Two distinct red lines appear. One line should be in the control line region (C) and another line should be in the test line region (T). A positive result means that IM heterophile antibodies were detected in the sample.
*NOTE: The shade of the red color in the test line region (T) will vary based on the amount of IM heterophile antibodies in the sample. Any shade of red in the test line region (T) should be considered positive.

NEGATIVE: One red line appears in the control line region (C). No apparent red or pink line appears in the test line region (T). A negative result means that IM heterophile antibodies were not found in the sample or are below the detection limit of the test.

INVALID: No line appears in the control line region (C). If this occurs, read the directions again and repeat the test with a new test cassette. If the result is still invalid, stop using the test kit and contact Alere Technical Support at (866) 216-0094.

QUALITY CONTROL

INTERNAL QUALITY CONTROL

Internal procedural controls are included in the test. A red line appearing in the control region (C) is an internal positive procedural control. It confirms sufficient sample volume, adequate membrane wicking and correct procedural technique. A clear background is an internal negative background control. If the test is working properly, the background in the result area should be white to light pink and not interfere with the ability to read the test result.

EXTERNAL QUALITY CONTROL

Quality control requirements must be performed in accordance with local, state, and federal regulations or accreditation requirements. Optimally, Alere recommends that positive and negative external controls be run with each new lot and with each new untrained operator. External positive and negative controls are supplied in the kit. Other commercial controls are not recommended if they have not been validated with this product.

PROCEDURE FOR EXTERNAL QUALITY CONTROL TESTING

Using the positive or negative external controls in place of a patient sample, add 1 drop of positive or negative control solution to the sample well (S) of a new test cassette, then add 1 drop of Sample Buffer. Start the timer. Continue with Step 3 in the Directions For Use section.

If unexpected results are seen when running the controls, review the Directions for Use, Interpretation of Results and Limitations sections and repeat the test with another cassette. If the problem persists, discontinue use of the test kit immediately and contact Alere Technical Support at (866) 216-0094.

LIMITATIONS

1. The Clearview MONO test (Whole Blood/Serum/Plasma) is for *in vitro* diagnostic use only. The test should be used for the detection of IM heterophile antibodies in whole blood, serum or plasma samples only. Neither the quantitative value nor the rate of increase in Mononucleosis antibody concentration can be determined by this qualitative test.
2. The Clearview MONO test will only indicate the presence of IM heterophile antibodies in the sample and should not be used as the sole criteria for the diagnosis of Mononucleosis infection.
3. Grossly hemolysed samples will yield invalid results. Strictly follow the Directional Insert instructions to obtain accurate results.
4. As with all diagnostic tests, all results must be interpreted together with other clinical information available to the physician.
5. This assay has not been established for patients under 18 years of age. A heterophile antibody response is observed in approximately 80-90% of adults and children with EBV-caused IM.[6]

EXPECTED VALUES

Epstein-Barr virus infection during adolescence or young adulthood causes infectious mononucleosis 35% to 50% of the time.[1,5]

The incidence of EBV-associated infectious mononucleosis in the USA has been estimated at 45 per 100,000 and is highest in adolescent and young adults- about 2 out of 1,000. No seasonal pattern of EBV infection exists. The incubation period is 10 to 60 days, though 7 to 14 days is common for children and adolescents.

PERFORMANCE CHARACTERISTICS

A total of 611 clinical samples were tested by three independent sites in a clinical study. Slide agglutination served as the reference method for the study. Serum, plasma and whole blood were also collected for the detection of IM heterophile antibodies by the Clearview MONO test.

Of the 611 clinical samples collected, 185 were considered positive and 426 clinical specimens were considered negative by slide agglutination method. The results for each sample matrix are summarized below.

SERUM

Clearview MONO	Slide agglutination +	Slide agglutination −
+	72	0
−	0	168

Positive Agreement = 72/72 > 99% (95%-100%)**
Negative Agreement = 168/168 > 99% (98%-100%)**

PLASMA

Clearview MONO	Slide agglutination +	Slide agglutination −
+	58	1
−	0	181

Positive Agreement = 58/58 > 99% (94%-100%)**
Negative Agreement = 181/182 > 99% (97%-99%)*

WHOLE BLOOD

Clearview MONO	Slide agglutination +	Slide agglutination −
+	50	0
−	5	76

Positive Agreement = 50/55 = 91% (80%-97%)*
Negative Agreement = 76/76 > 99% (95%-100%)**

ALL SPECIMENS

Clearview MONO	Slide agglutination +	Slide agglutination −
+	180	1
−	5	425

Positive Agreement = 180/185 = 97% (94%-99%)*
Negative Agreement = 425/426 > 99% (99%-99.99%)*
*Denotes 95% Confidence Interval
**Denotes 97.5% Confidence Interval

In addition, the clinical samples were tested with a commercially available rapid diagnostic test kit. 611 serum, plasma and whole blood specimens were used to compare the Clearview MONO test to a comparator test. The results showed a >99% agreement between the two test kits. The results for each sample matrix are summarized below.

SERUM

Clearview MONO	Comparator test +	Comparator test −
+	72	0
−	1	167

Positive Agreement= 72/73 = 99% (93%-99%)*
Negative Agreement= 167/167 > 99% (98%-100%)**

PLASMA

Clearview MONO	Comparator test +	Comparator test −
+	59	0
−	1	180

Positive Agreement= 59/60 = 98% (91%-99%)*
Negative Agreement= 180/180 > 99% (98%-100%)**

WHOLE BLOOD

Clearview MONO	Comparator test +	Comparator test −
+	50	0
−	1	80

Positive Agreement= 50/51 = 98% (90%-99%)*
Negative Agreement= 80/80 > 99% (96%-100%)**

ALL SPECIMENS

Clearview MONO	Comparator test +	Comparator test −
+	181	0
−	3	427

Positive Agreement = 181/184 = 98% (95%-99%)*
Negative Agreement = 427/427 > 99% (99%-100%)**
*Denotes 95% Confidence Interval
**Denotes 97.5% Confidence Interval

INTERFERENCE STUDIES

No interference with the Clearview MONO test results was observed in samples containing high levels of hemoglobin (up to 10 mg/mL), bilirubin (up to 1,000 mg/dL) and human serum albumin (up to 100 mg/mL).The test results were also unaffected when the hematocrit was altered ranging from 20% to 60% and when icteric and lipemic samples were tested.

POL STUDIES

Three physicians' offices were used to conduct an evaluation of the Clearview MONO test. Personnel with various educational backgrounds performed the testing. Each physician's office tested a randomly coded panel of samples consisting of negative (15), low positive (15), moderate positive (15) and invalid (15) for three days. The results obtained had a >99% correlation with the expected results.

NON-LABORATORY USER STUDY

A total of 77 untrained, inexperienced, non-laboratory participants were enrolled at three separate locations to demonstrate that they could follow the product instructions and perform the Clearview MONO test and obtain results similar to those obtained by trained laboratory technicians. Each participant received four blinded spiked whole blood samples: one negative, one invalid, one low positive and one medium positive.

Study participants were instructed to follow the Directional Insert and Procedure instructions to test the provided samples and record their test results. No other instruction or training was given. Upon completion of the test, participants filled out a brief questionnaire regarding the test procedure and ease of use of the labeling. The following results were obtained:

Site	Low Positive	Medium Positive	Negative	Invalid	Total Correct
A	23/27=85% (66-96%)*	25/27=93% (76-99%)*	27/27>99% (87-100%)*	27/27>99% (87-100%)*	102/108=94% (88-98%)*
B	25/27=93% (76-99%)*	25/27=93% (76-99%)*	27/27>99% (87-100%)*	27/27>99% (87-100%)*	104/108=96% (91-99%)*
C	23/23>99% (85-100%)*	23/23>99% (85-100%)*	23/23>99% (85-100%)*	23/23>99% (85-100%)*	92/ 92>99% (96-100%)*

*Denotes 95% Confidence Interval

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