

Lab Name:

Procedure #:

Procedure: CLIA Complexity: Moderate

Prepared By	Date Adopted	Supersedes Procedure #

Review Date	Revision Date	Signature

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This Procedural Bulletin is intended to provide a ready outline reference for performance of the assay. These abbreviated directions for use are not intended to replace the complete package insert. It is the obligation of every manufacturer of medical devices labeled FOR *IN VITRO* DIAGNOSTIC USE to provide a complete package insert in accordance with FDA labeling regulation (21 CFR 809.10). Prepared in accordance with the guidelines recommended by the Clinical and Laboratory Standards Institute, Wayne, PA 19087; CLSI Document GP2-A2.

Quidel Corporation provides CLSI procedures for your use. The procedures are required to include the same information as listed in the package insert. Any modifications to this document are the sole responsibility of the Laboratory.

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FOR USE BY HEALTH CARE PROFESSIONALS

CLIA Complexity: Moderate

INTENDED USE

The QuickVue+ Strep A test is intended for the rapid detection of Group A Streptococcal antigen directly from throat swabs and beta-hemolytic colonies recovered from culture. This test is intended for use as an aid in the diagnosis of Group A Streptococcal infection.

SUMMARY AND EXPLANATION

Group A *Streptococcus* is the most significant cause of pharyngitis. Early diagnosis and treatment of Group A Streptococcal pharyngitis has been shown to reduce the severity of symptoms and serious complications such as rheumatic fever and glomerulonephritis. Conventional culture methods require 24–48 hours for results.¹

PRINCIPLES OF THE PROCEDURE

QuickVue+ Strep A is a lateral-flow immunoassay, containing a highly specific and sensitive antibody to Group A Strep antigen.

To perform the test, a throat swab specimen is collected. Antigen is extracted from the swab specimen with Reagents A and B. The extracted sample is added to the Test Cassette.

If the sample contains Strep A antigen, a pink vertical line (|) forms in the Read Result Window. This pink vertical line, together with the pre-printed blue horizontal line (–), forms a plus sign (+) to indicate a positive result. If Strep A is not present in the sample, the Read Result Window shows only the pre-printed blue horizontal line, forming a minus sign (–) to indicate a negative result.

As the sample continues to move through the test, the Control Window containing Strep A antigen becomes pink. Pink color in the Control Window indicates that the detection antibody is functionally active and is also evidence that the detection part of the test is functioning properly.

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The appearance of blue color in the Test Complete Window indicates the completion of the test. This occurs approximately 5 minutes after the addition of the extracted sample to the Test Cassette.

REAGENTS AND MATERIALS PROVIDED

- Individually Packaged Test Cassettes (25): Rabbit anti-Strep A antibody and heat-inactivated Strep A antigen
- Extraction Reagent A (1): 4 M Sodium Nitrite
- Extraction Reagent B (1): 0.2 M Acetic Acid
- Sterile Throat Swabs (25)
- Tubes and Tips (25)
- Positive Control (1): Heat-inactivated Group A *Streptococcus*, 0.02% sodium azide.
- Negative Control (1): Heat-inactivated Group C *Streptococcus*, 0.02% sodium azide.
- Package Insert (1)
- Procedure Card (1)

STORAGE AND STABILITY

Store kit at room temperature, 59–86°F (15–30°C). Kit contents are stable until the expiration date printed on the outer box. Do not freeze.

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Do not use kit contents after the expiration date printed on the outside of the kit.
- Use appropriate precautions in the collection, storage, handling, and disposal of patient samples and used kit contents.
- Use of Nitrile or Latex gloves is recommended when handling patient samples.²
- Dispose of containers and unused contents in accordance with Federal, State, and Local requirements.
- DO NOT interchange caps among reagents.

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- The Test Cassette must remain sealed in the foil pouch until just prior to use.
- Reagent A contains 27.6% sodium nitrite and may be harmful if ingested or absorbed.
- Reagent B contains an acidic solution. If the solution contacts the skin or eye, flush with large volumes of water.
- Do not use Reagent B if solution is green prior to mixing with Reagent A in the Tube. If this occurs, contact Quidel Technical Support.
- To obtain accurate results, you must follow the Package Insert instructions.

SPECIMEN COLLECTION AND STORAGE

Collect throat swab specimens by standard clinical methods. When swabbing the throat, be careful not to touch the tongue, sides or top of the mouth with the swab. Rub the swab on the back of the throat, on the tonsils and in any other area where there is redness, inflammation or pus. Bloody specimens can create an interfering background and can cause an invalid result. Consult reference procedures such as the collection method described by Facklam.³

Use rayon-tip or dacron-tip swabs with plastic shafts; individually packaged sterile rayon-tipped swabs are provided in the kit. Do not use calcium alginate, cotton-tip or wooden shafted swabs. Swab specimens should be processed as soon as possible after collection. However, swabs can be stored in a clean, dry, sealable plastic tube or in 1 mL or less liquid media, such as modified Stuart's Transport Media, for up to eight hours at room temperature (15–30°C) or 72 hours refrigerated (2–8°C). Do not use charcoal agar or semi-solid transport media.

If culture results are also desired, lightly streak the swab on a 5% sheep blood agar plate before using the QuickVue+ Strep A test. The culture plate must be streaked prior to running the QuickVue+ test, as the reagents will kill the bacteria on the swab. Throat swab specimens can also be obtained by dual swabs or by two swabs taken in sequence for the culture procedure.

CULTURE CONFIRMATION

The QuickVue+ Strep A test can be used to confirm the identification of Group A Streptococcus on SBA culture plates. Lightly touch a colony using a sterile swab. Do not sweep the plate. Follow the instructions in the TEST PROCEDURE section to test the sample.

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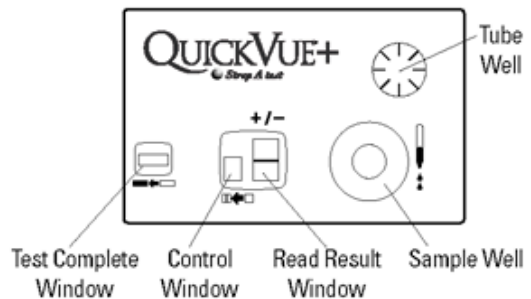
TEST PROCEDURE

Important: Gloves should be worn when handling human samples.

BEFORE TESTING

- Remove the Test Cassette from the foil pouch and place it on a level surface.

- Put a clean tube in the Tube Well of the Test Cassette. Squeeze **4 DROPS** of Reagent A and **4 DROPS** of Reagent B into the tube. The solution should turn green once Reagent B is added.



- **Note:** when adding drops, hold bottle vertically so that a complete drop forms.

- Immediately place the throat swab into the tube. Mix solution thoroughly by swirling the swab five (5) times (or vortex briefly).

- **Wait one (1) minute.**

- Remove the tube from the Tube Well. Express all liquid from the swab head by rolling the swab against the inside of the tube and **squeezing firmly** as it is withdrawn from the tube. Discard the swab.

- Put a clean tip on the tube.

PERFORM TEST

- Add **2 DROPS** from the Tube to the round Sample Well in the Test Cassette.
- For a valid result the test must be read in 10 minutes or less after adding the sample and there must be ANY shade of blue in the Test Complete Window.
- If there is no shade of blue in the Test Complete Window at 10 minutes, the result is invalid.

INTERPRETATION OF RESULTS

Positive Results may be read as early as 5 minutes after or as late as ten minutes after adding the sample.

Negative Results at five minutes must be confirmed negative at 10 minutes.

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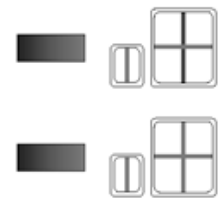
Positive Result:

The sample contains Group A *Streptococcus* antigen when you see:

- A pink and blue plus sign (+) in the large square Read Result Window along with a pink color in the small square Control Window

AND

- Any shade of blue color in the Test Complete Window



Note: the combination of any shade of a pink vertical line in the Read Result Window and any blue shade in the Complete Result Window should be interpreted as a positive result.

Negative Result:

The sample does not contain Group A *Streptococcus* antigen when you see **at 10 minutes** after adding the sample:

- A blue minus sign (-) in the large square Read Result Window along with a pink color in the small square Control Window

AND

- Any shade of blue color in the Test Complete Window



Note: A negative QuickVue+ result indicates a presumptive negative test result for the presence of Group A *Streptococcal* antigen.

Invalid Result:

The result is invalid if:

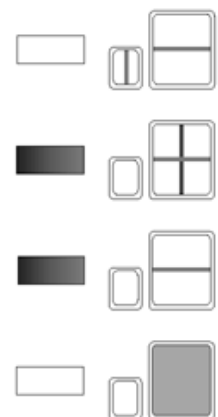
- At 10 minutes, no shade of blue appears in the Test Complete Window

OR

- No pink color appears in the Control Window by 10 minutes

OR

- Background color in the Read Result Window interferes with test interpretation at 10 minutes



Note: In the case of an invalid result, a new patient sample should be tested using a new QuickVue+ Strep A test, or contact Quidel Technical Support.

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QC TESTING PROCEDURE

- Follow the instructions in the TEST PROCEDURE to dispense the Extraction Reagents into the tube.
- Vigorously mix the Control Bottles. Add one (1) drop of the Negative **or** Positive Control into the tube.
- Place a clean swab into the tube and follow the instructions for testing the patient swab.

QUALITY CONTROL

Built-in Control Features

The QuickVue+ Strep A provides three levels of internal procedural controls with each test run. For daily quality control, Quidel recommends documenting that these internal controls were checked for the first sample tested each day.

Built-in Extraction Reagent Control: The color of the Extraction Reagent changes from clear to green as the reagents are mixed together. The color change is an internal extraction reagent control and is an indication that the reagents were mixed and functioning properly.

Built-in Positive Antigen Control: Pink color in the Control Window serves as a built-in positive antigen control. The appearance of this control indicates that the detection antibody is functionally active and is also evidence that the detection part of the test is functioning properly.

Built-in Negative Background Control: The background area in the Read Result Window should be white to light pink within 10 minutes and not interfere with the reading of the result. A lack of interfering background serves as a built-in negative background control, indicating that there are no immunological interfering substances in the sample.

External Quality Control Testing

External controls are provided and may also be used to ensure that the reagents are performing properly and that you are able to correctly perform the test procedure. You may also use controls derived from ATCC strain 19615. Some commercial controls may contain interfering additives and are not recommended for use in the QuickVue+ test.

Positive and negative controls can be run with each shipment of a new kit lot number, and as otherwise required by your laboratory's standard quality control procedures.

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LIMITATIONS OF THE PROCEDURE

The contents of this kit are for use in the qualitative detection of Group A Streptococcal antigen from throat swabs and culture colonies only.

Respiratory infections, including pharyngitis, can be caused by *Streptococcus* from serogroups other than Group A as well as other pathogens. The QuickVue+ test will not differentiate asymptomatic carriers of Group A *Streptococcus* from those exhibiting Group A Streptococcal infection.

In rare cases, test specimens heavily colonized with *Staphylococcus aureus* can yield false positive results.

Test results must always be evaluated with other data available to the physician. A negative test result might occur if the level of extracted antigen in a sample is below the detection level of the test. Additional follow-up testing using the culture method is recommended if the QuickVue+ test result is negative.⁴

EXPECTED VALUES

Group A *Streptococci* cause about 19% of all upper respiratory tract infections. Streptococcal pharyngitis is seasonal in nature with the highest prevalence found during the winter and early spring. The highest incidence of this disease is found in crowded populations such as military bases and in school-aged children, and is evenly distributed between males and females.⁵

PERFORMANCE CHARACTERISTICS

Clinical Sensitivity and Specificity

A multi-center evaluation of the QuickVue+ Strep A test was conducted to determine the clinical performance of the test relative to standard sheep blood agar (SBA) culture techniques. Throat swab specimens were collected from patients presenting with pharyngitis. Prior to performance of the QuickVue+ test, each swab specimen was inoculated onto a SBA culture plate containing a bacitracin disk and incubated at 37°C anaerobically for 24–48 hours for evaluation. All cultures were confirmed for the presence of Group A *Streptococcus* using commercial latex agglutination assays.

Of the 719 specimens that were found negative by SBA culture, 707 were also negative by the QuickVue+ test. Similarly, of the 114 specimens that were confirmed SBA culture positive, 108 were also positive by the QuickVue+ test. The QuickVue+ test correctly identified 100% (5/5) of the 1+ cultures; 95% (20/21) of the 2+ cultures; 100% (31/31) of the 3+ cultures; and 98% (52/53) of the 4+ cultures. The 4 culture positive specimens with less than 10 colonies (rares) were not positive by the QuickVue+ test. Based on this data, **specificity was 98%** and **sensitivity was 95%** for the QuickVue+ test. 95% confidence intervals were calculated to be 97–99% and 91–99% for specificity and

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sensitivity, respectively. **Overall agreement between SBA culture and QuickVue+ Strep A was 98% (815/833).**

In addition, the QuickVue+ Strep A test was used to confirm the identification of Group A Streptococcus on SBA culture plates. As a culture confirmation, the QuickVue+ test was 100% sensitive and 100% specific.

Physician's Office Laboratory (POL) Studies

An additional evaluation of the QuickVue+ test was conducted at three physicians' offices using a panel of coded samples. Testing was performed by physician's office personnel with diverse educational backgrounds and work experience. The panel contained negative, low positive and moderate positive samples. Each sample level was tested in sets of five at each site over a period of three days.

The results obtained at each site ranged from 97% to 100% agreement with the expected results. No significant differences were observed within run, between runs or between sites.

Cross-Reactivity

Cross-reactivity studies with 53 microorganism strains other than Group A *Streptococcus* have been performed at levels exceeding 10^7 and produced negative results in the QuickVue+ test.

ASSISTANCE

If you have any questions regarding the use of this product, please call Quidel's Technical Support Number (800) 874-1517 (toll-free in the U.S.A.) or (858) 552-1100, Monday through Friday, between 7:00 a.m. and 5:00 p.m. Pacific Time, U.S.A. If outside the United States, contact your local distributor or technicalsupport@quidel.com.

REFERENCES

1. Ruoff, K. *Streptococcus*. In: *Manual of Clinical Microbiology*, Murray, PR ed. 6th Edition, 1995, 23: 301.
2. Biosafety in Microbiological and Biomedical Laboratories, 4th Edition. U.S. Department of Health and Human Services, CDC, NIH, Washington, D.C. (1999).
3. Facklam, RR and Washington II, JA. *Streptococcus* and Related Catalase-Negative Gram-Positive Cocci. In: *Manual of Clinical Microbiology*, Balows, A ed. 5th Edition, 1991, 29: 241.

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4. American Academy of Pediatrics. Group A Streptococcal Infections. In: *1994 Redbook: Report of the Committee on Infectious Diseases*. Peter, G. ed. 23rd Edition, Elk Grove, IL, 1994, p 433.
 5. Wannamaker, LW. *New England Journal of Medicine*, 1970, 282: 23-31.
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REF

20122 - QuickVue+ Strep A 25-Test Kit

IVD**EC REP**

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QUIDEL[®]

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EC REP Authorized Representative in the European Community	REF Catalogue number
CONTROL + Positive control	CONTROL - Negative control
 Use by	IVD For <i>In Vitro</i> diagnostic use
LOT Batch code	 Consult instructions for use
 Manufacturer	 Temperature limitation

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LOG SHEET



Record Built-in Procedural Controls on the first patient tested each day.

	Date	Patient Name	Negative Procedural Control (Clear Bkgd)	Positive Procedural Control (Pink Line)	Test Results At 5 minutes	Lot Number/Exp. Date	Technician
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							
11							
12							
13							
14							
15							

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LOG SHEET



Need to run external Positive and Negative controls once per lot or shipment of material per CLIA package insert requirements.

	Date/Date Received	External Positive Controls	External Negative Controls	Lot Number/Exp. Date	Technician
1					
2					
3					
4					
5					
6					
7					
8					
9					
10					
11					
12					
13					
14					
15					