Alere™

Alere™ i Strep A 2 Package Insert

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For use with the **Alere™ i** Instrument
For use with throat swab specimens
For *in vitro* use only
℞ Only

CLIA COMPLEXITY: WAIVED

A Certificate of Waiver is required to perform this test in a CLIA Waived setting. To obtain CLIA waiver information and a Certificate of Waiver, please contact your state health department. Additional CLIA waiver information is available at the Centers for Medicare and Medicaid website at www.cms.hhs.gov/CLIA.

Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for waived classification and being classified as high complexity.

INTENDED USE

Alere™ i Strep A 2 is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of *Streptococcus pyogenes*, Group A *Streptococcus* bacterial nucleic acid in throat swab specimens obtained from patients with signs and symptoms of pharyngitis. It is intended to aid in the rapid diagnosis of Group A *Streptococcus* bacterial infections.

SUMMARY AND EXPLANATION OF THE TEST

Streptococcus pyogenes, Group A Strep is the most significant pathogen causing pharyngitis. Accurate diagnosis of the etiological agent is necessary to properly treat the disease. In the case of Group A Strep, antibiotic therapy is the treatment of choice. If left untreated, serious complications such as rheumatic fever may occur.[1]

Conventional methods for detecting Group A Strep infection include rapid antigen testing or 24-48 hour culture of throat swab specimens followed by confirmation of beta-hemolytic colonies as Group A Strep.[1] Rapid antigen test sensitivities are variable and follow-up throat culture to confirm negative results is recommended. When an adequate throat swab specimen is obtained and cultured by trained personnel false-negative culture results occur in fewer than 10% of symptomatic patients.[2]

Alere™ i Strep A 2 is a rapid, instrument-based isothermal test for the qualitative detection of Group A Strep directly from throat swab specimens with results in six (6) minutes or less. The **Alere™ i** Instrument has a small footprint and easy to use graphical user interface for convenience within a busy hospital or point-of-care environment. The **Alere™ i** Strep A 2 kit contains all components required to carry out an assay for Group A Strep on the **Alere™ i** Instrument.

PRINCIPLES OF THE PROCEDURE

Alere™ i Strep A 2 utilizes isothermal nucleic acid amplification technology for the qualitative detection of Group A Strep bacterial nucleic acids. It is comprised of a Sample Receiver, containing elution buffer, a Test Base, comprising two sealed reaction tubes, each containing a lyophilized pellet, a Transfer Cartridge for transfer of the eluted sample to the Test Base, and the **Alere™ i** Instrument.

The reaction tubes in the Test Base contain the reagents required for Group A Strep bacterial lysis and the subsequent amplification of the target nucleic acid and an internal control. **Alere™ i** Strep A 2 utilizes templates (similar to primers) for the specific amplification of DNA from Group A Strep and a fluorescently-labelled molecular beacon designed to specifically identify the amplified nucleic acid target.

To perform the assay, the Sample Receiver and Test Base are inserted into the **Alere™ i** Instrument. The sample is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, initiating bacterial lysis and target amplification. Heating, mixing and detection are provided by the instrument, with results automatically reported.

REAGENTS AND MATERIALS

Materials Provided

Test Bases: BASE	Orange plastic components containing two reaction tubes of lyophilized reagents. One tube contains reagents for the targeted amplification of Group A Strep nucleic acid and the other tube contains the internal control.
Sample Receivers: RCVR	Blue plastic components containing 2.5 mL of elution buffer.
Transfer Cartridges: CARTRDG	White plastic components used to transfer 2 x 100 µL of sample extract from the Sample Receiver to the Test Base.
Throat Swabs:	Sterile swabs for use with the **Alere™ i** Strep A 2 Test.
Positive Control Swab:	The positive control swab is coated with inactivated Group A Strep bacteria.
Negative Control Swab:	The negative control swab is coated with inactivated Group C Strep.
Package Insert	
Quick Reference Instructions	

Materials Required but not Provided

Alere™ i Instrument

Clean, dry plastic tubes or sheaths for transport and storage of swab specimens.

PRECAUTIONS

1. For *in vitro* diagnostic use.
2. For US Customers Only: Federal Law restricts this device to sale by or on the order of a licensed practitioner.
3. To be used in conjunction with the **Alere™ i** Instrument.
4. Leave test pieces sealed in their foil pouches until just before use.
5. Do not tamper with test pieces prior to use.
6. Do not use kit past its expiration date.
7. Do not mix components from different kit lots.
8. Solutions used to make the control swabs are inactivated using standard methods. However, patient samples, controls, and test pieces should be handled as though they could transmit disease. Observe established precautions against microbial hazards during use and disposal.
9. **If any assay components are dropped, cracked, found to be damaged or opened when received, DO NOT USE and discard. Do not use scissors or sharp objects to open foil pouches as damage to test pieces can occur. Do not touch the test tubes contained within the Test Base.**
10. Do not use a Transfer Cartridge if it is dropped after aspiration of the sample. If the Transfer Cartridge is dropped, discard the component and continue the test by transferring the sample with a new Transfer Cartridge.
11. Do not open the Sample Receiver before placing in the instrument.
12. If the Sample Receiver is spilled while opening, clean the instrument per instructions provided in the instrument User Manual and cancel test. Repeat test with a new Sample Receiver.
13. All test pieces must be removed from the instrument according to removal instructions displayed on the instrument, and disposed of according to country and local requirements. **Pieces must not be separated once they are assembled.**
14. All test pieces are single use items. Do not use with multiple specimens.
15. Once reacted, the Test Base contains large amounts of amplified target (Amplicon). Do not disassemble the Test Base and Transfer Cartridge. In the case of a positive sample, this could lead to amplicon leakage and potential **Alere™ i** Strep A 2 false positive test results.
16. At a very low frequency, clinical samples can contain inhibitors that may generate invalid results.
17. Due to the high sensitivity of the assays run on the instrument, contamination of the work area with previous positive samples may cause false positive results. Handle samples according

to standard laboratory practices. Clean instruments and surrounding surfaces according to instructions provided in the cleaning section of the instrument User Manual. Refer to Section 1.6, Maintenance & Cleaning, for further information.

18. Do not touch the heads of the Control Swabs. Cross contamination with the Positive Control Swabs may occur due to their high target level and the sensitivity of the assays run on the instrument.
19. Test results should be interpreted in conjunction with other laboratory and clinical data.
20. The performance of **Alere™ i** Strep A 2 was evaluated using the procedures provided in this package insert only. Modifications to these procedures may alter the performance of the test.
21. False negative results may occur if a specimen is improperly collected, transported or handled; or if inadequate quantities of target DNA are present in the system.
22. To avoid contamination, do not move the **Alere™ i** Instrument during a run or until all assay components have been removed from the instrument.
23. The orange indicator should rise when the Transfer Cartridge is pressed into the Sample Receiver until a click is heard. The indicator should descend fully when correctly connected to the Test Base. Failure to follow this procedure may lead to false negative or invalid results.
24. As with other assays of this type, there is a risk of false negative or invalid results due to the presence of sequence variants in the amplification targets.

STORAGE AND STABILITY

Store kit at 2- 30˚C. The **Alere™ i** Strep A 2 kit is stable until the expiration date marked on the outer packaging and containers. Ensure all test components are at room temperature before use.

QUALITY CONTROL

Alere™ i Strep A 2 has built-in procedural controls. The result of the Procedural Control is displayed on the screen and is automatically stored in the instrument with each test result. This can be reviewed later by selecting Review Memory on the instrument.

Procedural Controls:

Alere™ i Strep A 2 contains an internal control that has been designed to control for the functionality of the amplification / detection process and reagents. In positive samples where target amplification is strong, the internal control is ignored and the target amplification serves as the ‘control’ to confirm that the clinical sample was not inhibitory and that assay reagent performance was robust. At a low frequency, clinical samples can contain inhibitors that may generate invalid results.

Procedural Control Valid displayed on the instrument screen indicates that the assay reagents maintained their functional integrity and the sample did not significantly inhibit assay performance.

External Positive and Negative Controls:

Good laboratory practice suggests the use of positive and negative controls to ensure that test reagents are working and that the test is correctly performed. **Alere™ i** Strep A 2 kits contain Positive and Negative Control Swabs. These swabs may be used to demonstrate the ability to generate appropriate positive and negative results by following the assay process. Test these swabs once when the assay is run on an instrument for the first time, as well as with each new shipment received and once for each untrained operator. Further controls may be tested in order to conform with local, state and/or federal regulations, accrediting groups, or your lab's standard Quality Control procedures.

CONTROL SWAB PROCEDURE

External Positive and Negative Control swabs are provided and should be tested following the Run QC Test instructions on the **Alere™ i** Instrument. Refer to Test Procedure or Instrument User Manual for further details.

If the correct control results are not obtained, do not perform patient tests or report patient results. Contact Technical Support during normal business hours before testing patient specimens.

SPECIMEN COLLECTION AND HANDLING

Use freshly collected specimens for optimal test performance. Inadequate specimen collection or improper sample handling/ storage/transport may yield erroneous results.

Specimen Collection

For optimal performance, use the swabs provided in the test kit. Alternatively, foam, polyester, HydraFlock® and nylon flocked throat swabs can be used to collect throat swab samples. The BBL™ CultureSwab™ Liquid Amies transport media system has been tested and is also acceptable.

Rayon swabs and the BBL™ CultureSwab™ Liquid Stuart transport media system are not suitable for use in this assay.

Collect patient specimen by swabbing the posterior pharynx, tonsils and other inflamed areas. Avoid touching the tongue, cheeks and teeth with the swab.[3]

SPECIMEN TRANSPORT AND STORAGE

Swab specimens should be tested as soon as possible after collection. If immediate testing is not possible, the throat swab can be held in its original package or a clean, dry plastic tube or sleeve at room temperature (approximately 22°C) or refrigerated at 2-8°C for up to seventy-two (72) hours prior to testing.

The collection swab is to be tested following the step-by-step instructions shown on the instrument screen. If immediate testing is not possible, the transport media system can be held at room temperature (approximately 22°C) or refrigerated at 2-8°C for up to six (6) hours prior to testing.

TEST PROCEDURE

Before testing with **Alere™ i** Strep A 2:

- Allow all samples to reach room temperature
- Allow all test pieces to reach room temperature
- Check that a reagent pellet is visible at the bottom of each of the reaction tubes prior to inserting the Test Base in the **Alere™ i** Instrument. Do not use the Test Base if a pellet is not visible at the bottom of each reaction tube.

To Perform Test:

1. Follow the step-by-step instructions shown on the instrument screen.

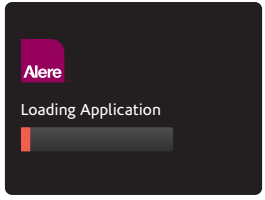
Note: If testing a swab transported in media, the collection swab is to be tested following the step-by-step instructions shown on the instrument screen.

*Note: The optimum environmental operating conditions for **Alere™ i** Strep A 2 are: 15-30°C and 10-80% relative humidity.*

Step 1

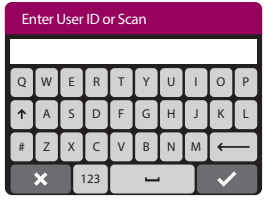
Turn on the **Alere™ i** Instrument - press the power button ⏻ on the side of the instrument.

Note: If the unit is unattended for one hour, the instrument will go to a black screen power save mode. Touch the screen to return the unit to active display operation.



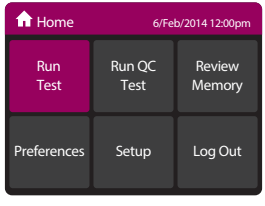
Enter User ID

Press '✓' after entry.



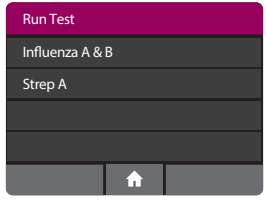
Touch 'Run Test'

This will begin the test process.



Touch 'Strep A'

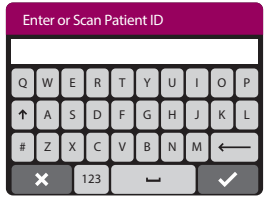
This starts a Strep A test.



Enter Patient ID using on screen keyboard or barcode scanner

Touch '✓'.

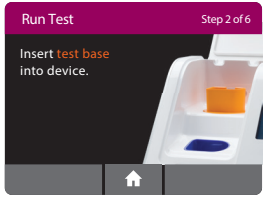
Verify that the ID was entered correctly, then touch '✓' to confirm entry.



Step 2

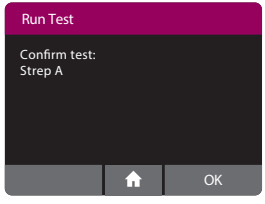
Open the Lid and Insert Orange Test Base into Orange Test Base holder

⚠ Caution: Do not apply excessive force. Excessive force could damage the instrument.



Confirm that the correct test is displayed on the screen.

Touch ‘OK’ to proceed.



⚠ Caution: Once the Test Base has been placed in the holder, the user will have 10 minutes to confirm the test. If the test is not confirmed within 10 minutes, the instrument will time out and the Test Base must be removed and discarded.

If the incorrect Test Base has been inserted, remove and dispose of the incorrect Test Base. Close the lid. The instrument will then run a self-test before proceeding to the Home screen. Press Run Test and restart the test using the correct Test Base.

Step 3

Insert Blue Sample Receiver into the Blue Sample Receiver holder

⚠ Caution: Do not apply excessive force. Excessive force could damage the instrument.

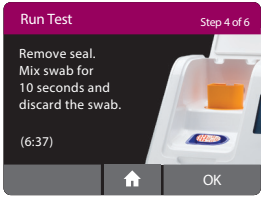
⚠ Caution: Confirm that the Sample Receiver foil pouch indicates that it is for use with Alere™ i Strep A 2 (not another Alere™ i assay). Confirm that the foil seal on the Sample Receiver is for the Strep A assay. If not, then remove the Sample Receiver and replace it with a new Sample Receiver for Alere™ i Strep A 2.

⚠ Caution: Once the Sample Receiver has been placed in the holder, the user will have 10 minutes to start the test (Steps 3 through 5). If the test is not started within 10 minutes, the instrument will time out and all test pieces (Test Base and Sample Receiver) must be removed and discarded. The instrument will proceed to the Home screen. Press Run Test and restart the test using a new Test Base and Sample Receiver.

Step 4

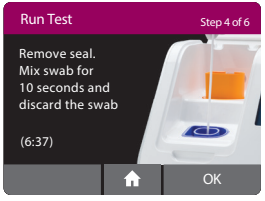
When prompted, remove the foil seal and place the patient swab to be tested into the Sample Receiver.

⚠ Caution: To ensure the Sample Receiver remains in the instrument while removing the foil seal, place two fingers along the outer edge of the Sample Receiver to hold it in place. If the Sample Receiver spills after warm up, cancel the test by pressing the Home button. Remove and discard the test pieces (Sample Receiver and Test Base) and clean the instrument. Press Run Test to start a new test using a new Test Base and Sample Receiver.



Vigorously mix the swab in the liquid for 10 seconds. Press the swab head against the side of the Sample Receiver as you mix it. This helps remove the sample from the swab. Once the swab is removed, touch ‘OK’ to proceed.

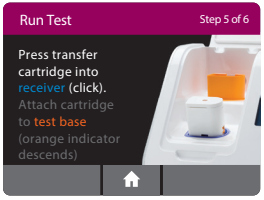
Discard the swab.



Step 5a

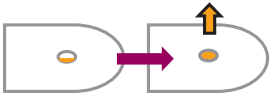
Press the White Transfer Cartridge into the Blue Sample Receiver

Listen for a click.



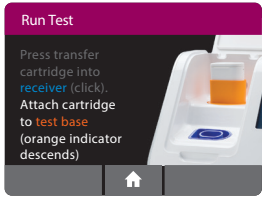
When the Transfer Cartridge is properly attached to the Sample Receiver, the orange indicator on the Transfer Cartridge will rise. If the orange indicator does not rise, continue pushing onto the Sample Receiver until it does.

⚠ Caution: The orange indicator should be observed closely. If the orange indicator does not fully rise, the Transfer Cartridge may not collect enough sample and may lead to false negative or invalid results.



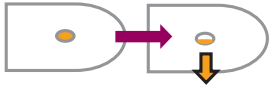
Step 5b

Lift and then connect the Transfer Cartridge to the Test Base



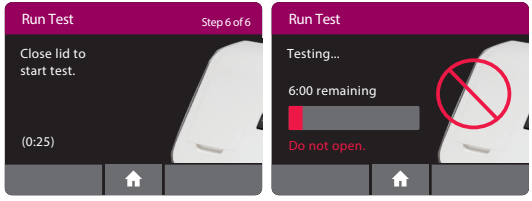
When the Transfer Cartridge is properly attached to the Test Base, the orange indicator on the Transfer Cartridge will descend. If the orange indicator does not descend, continue pushing onto the Test Base until it does.

⚠ Caution: If the orange indicator does not fully descend, not enough sample will be dispensed. This may potentially result in invalid or false negative results.



Step 6

Close the Lid.



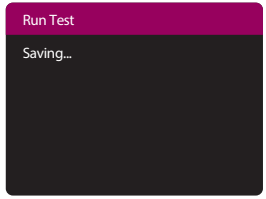
DO NOT OPEN THE LID until the **Test Complete** message appears on the screen.

Note: The test will be cancelled if the lid is opened.

⚠ **Caution: This screen will be displayed for up to 30 seconds once the Transfer Cartridge is detected. If the instrument does not detect that the lid has been closed by then, it will time out and all test pieces (Sample Receiver, Test Base, and Transfer Cartridge) must be removed and discarded. The instrument will proceed to the Home screen. Collect a new sample from the patient. Press Run Test and restart the test using a new Test Base and Sample Receiver.**

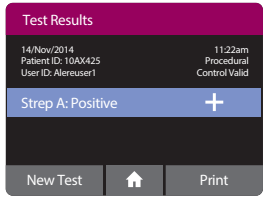
⚠ **Caution: DO NOT OPEN THE LID. The test will be cancelled and all test pieces (Sample Receiver, Test Base, and Transfer Cartridge) must be removed and discarded. A test result will not be reported or saved in the instrument memory.**

When amplification and detection is complete, the instrument will automatically save the data before advancing to the results screen.



⚠ **Caution: The test is not saved until the completed result is displayed. Do not open the lid until the results are displayed.**

The **Test Results** screen displays either a Negative or Positive result for a successfully completed test. If a test error occurs, the display will read 'Invalid'. Refer to the Result Interpretation Section for Interpretation of Results.



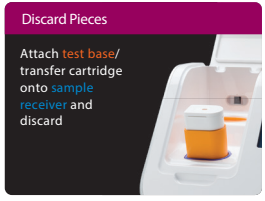
Press Print to print test results, press New Test to run another test, Press Home to return to the Home screen

After printing, or if New Test or Home are selected, the instrument will prompt to open the lid and discard the used test pieces.

Remove test pieces by lifting the Transfer Cartridge attached to the Test Base, and clicking it into the Sample Receiver, by pressing into the Sample Receiver.

⚠ Caution: Do not try to remove the Sample Receiver by any other method as there is a risk of spilling the patient sample.

All test pieces will be connected and can now be removed from the instrument and disposed of according to federal, state and local regulations.

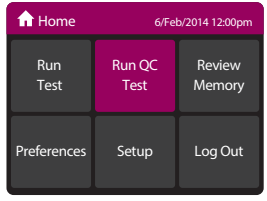


⚠ Caution: DO NOT disassemble the Transfer Cartridge and the Test Base before disposal.

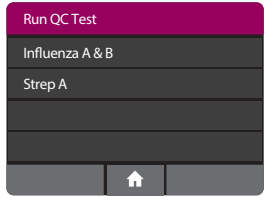
Close the lid. The instrument will then run a Self-Test before showing the Home screen or Enter Patient ID screen, depending on the previous selection.

Quality Control Swab Test Procedure:
For QC testing, select Run QC Test on the Home screen, and follow the displayed instructions. Refer to Running a QC Test in the **Alere™ i** Instrument User Manual for further details.

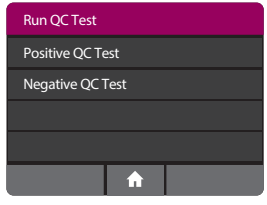
1. Touch 'Run QC Test'



2. Touch 'Strep A'

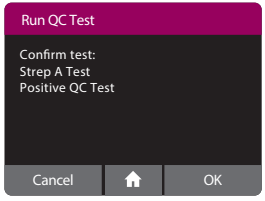


3. Select the QC Test to be Run



4. Confirm Test

Confirm the test type to match the QC sample intended for testing by touching ‘OK’ and following the on screen prompts to complete testing.



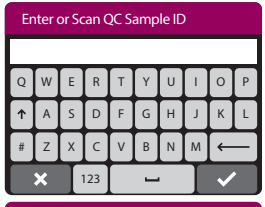
5. QC Sample ID

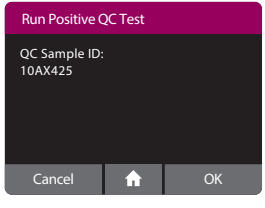
The user has the option to enter an ID for the QC Sample being run.

Enter or Scan QC Sample ID. Press ‘✓’ to confirm.

The QC Sample ID entered will be displayed. Press OK to confirm or cancel to reenter.

If it is not desired to enter or scan in the QC sample ID leave blank and press ‘✓’ to continue.

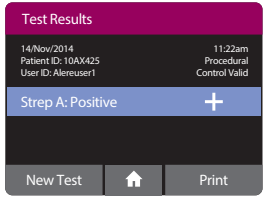
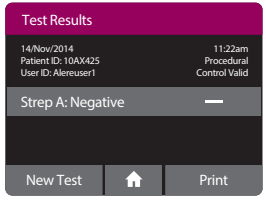
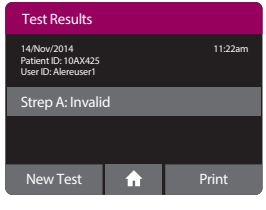




*Note: The QC test is run in the same manner as a Patient Test. See the **To Perform a Test** section above for step by step instructions.*

RESULT INTERPRETATION

When the test is complete, the results are clearly displayed on the instrument screen.

Instrument Display	Suggested Report
	**Positive for Strep A nucleic acid.**
	**Negative for Strep A nucleic acid.**
	**Invalid.** Immediately repeat testing of the sample using new test components. If repeated Invalid results are obtained, repeat test with a new patient sample and new test components.

If an Invalid result is received, one additional test may be run using the same Sample Receiver. The instructions below should be followed:

- Remove the connected Test Base and Transfer Cartridge from the instrument and connect the Test Base portion to an UNUSED Sample Receiver. The connected Test Base and Transfer Cartridge MUST be attached to a Sample Receiver prior to disposal. The Sample Receiver from a new Transfer Cartridge package may be used for this.
- Remove the blue Sample Receiver separately and carefully from the instrument. The Sample Receiver should be retained and kept upright, to avoid spilling the liquid contents.
- From the Home Screen, start a new test. Follow the screen prompts, however when asked to insert the Sample Receiver, reuse the Sample Receiver and DO NOT re-elute the swab.

LIMITATIONS

- For optimal performance, use the specimen collection swabs provided in the test kit. Analytical studies have demonstrated that rayon swabs and BBL CultureSwab Liquid Stuart Medium are not suitable for use with this assay and may produce false negative results.
- **Alere™ i** Strep A 2 does not distinguish between viable and nonviable organisms.
- Performance of **Alere™ i** Strep A 2 has not been established for monitoring treatment of pharyngitis caused by Group A Strep.
- **Alere™ i** Strep A 2 will not differentiate asymptomatic carriers of Group A Strep from those exhibiting streptococcal infection.
- False results may occur if a Sample Receiver for an assay other than **Alere™ i** Strep A 2 is used.
- Additional follow-up testing using the culture method is required if the result is negative and clinical symptoms persist, or in the event of an acute rheumatic fever (ARF) outbreak.

EXPECTED VALUES

Overall incidence of Group A Strep in patients tested during the 2017 clinical study was 20.2% (198/981) as determined by the reference culture procedure and 25.2% (247/981) as determined by **Alere™ i** Strep A 2.

PERFORMANCE CHARACTERISTICS

Clinical Study:

The clinical performance of **Alere™ i** Strep A 2 was established in a multi-center, prospective clinical study conducted at 9 US trial sites in 2017.

A total of 981 evaluable throat swab specimens, collected from patients of all ages presenting with symptoms of pharyngitis, were evaluated with **Alere™ i** Strep A 2 and compared to bacterial culture. 53 (5.4%) patients tested were ≤ 3 years of age, 425 (43.3%) were 3-12 years of age, 200 (20.4%) were 13–20 years of age and 303 (30.9%) were > 20 years.

The study population included 582 (59.3%) female patients and 399 (40.7%) male patients. No performance differences were noted based on age or gender.

In this study, two (2) throat swabs were collected from each of a total of 981 evaluable patients. One throat swab from each patient was tested with **Alere™ i** Strep A 2. The other throat swab was sent to a central laboratory for bacterial culture.

Alere™ i Strep A 2 performance, including 95% confidence intervals, versus bacterial culture is provided below.

Alere™ i Strep A 2 Performance vs. Culture

	Culture +	Culture -	
Alere™ i +	195	52[a]	247
Alere™ i -	3[b]	731	734
	198	783	981

Sensitivity: 195/198 = 98.5% (95% CI = 95.6%, 99.5%)
Specificity: 731/783 = 93.4% (95% CI = 91.4%, 94.9%)
Positive Predictive Value = 195/247 = 78.9% (95% CI = 74.3%, 83.6%)
Negative Predictive Value = 198/734 = 99.6% (95% CI = 98.3%, 99.9%)
Prevalence: 198/981 =20.2% (95% CI = 17.8%, 22.8%)

[a] Of the 52 samples positive by **Alere™ i** Strep A 2 and negative by bacterial culture, 38 were also positive for Group A Strep by a laboratory developed real-time PCR assay and

[b] Of the 3 samples negative by **Alere™ i** Strep A 2 and positive by bacterial culture, 1 sample was also negative for Group A Strep by a laboratory developed real-time PCR assay.

During the prospective clinical study, the initial invalid rate (before repeat testing per the product instructions) was 0.9% (9/985) (95% CI: 0.5%, 1.7%). After repeat testing per the product instructions, the invalid rate was 0.4% (4/985) (95% CI: 0.2%, 1.0%).

Analytical Studies:

Reproducibility

A reproducibility study of **Alere™ i** Strep A 2 was conducted by operators from 3 sites using panels of blind coded specimens containing negative, low positive (~2X the limit of detection), and moderate positive (~3X the limit of detection) Group A Strep bacterial samples. Participants tested multiple samples of each panel member on 5 different days.
The percent agreement with expected results for the Group A Strep moderate positive and low positive samples were both 100% (90/90). All of the negative samples (90) generated negative test results. There were no significant differences within run (replicates tested by one operator), between run (5 different days), between sites (3 sites), or between operators (9 operators).

Analytical Sensitivity (Limit of Detection)

Alere™ i Strep A 2 limit of detection (LOD or C_{95}), defined as the concentration of Group A Strep that produces positive **Alere™ i** Strep A 2 results approximately 95% of the time, was identified by evaluating different concentrations of Group A Strep in **Alere™ i** Strep A 2. The concentrations identified as the LOD (or C_{95}) level for each strain tested are listed in the following table.

Group A Strep Strain	Concentration (cells/mL of Elution Buffer)[1]	% Detected
ATCC 12344	147	100%
ATCC 19615	25	95%

[1] As determined by correlation of optical density of cell stocks with microscopy chamber counts

Analytical Reactivity

The following Group A Strep strains were tested and produced positive results at or near the stated assay limit of detection of the **Alere™ i** Strep A 2 test: ATCC8135, ATCC12384, ATCC12202, ATCC12203, ATCC12204, ATCC12365, ATCC14289, ATCC49399, ATCC51339, ATCC700294, ATCC12357, ATCC12385 Loomis, ATCC 12385 Type 4, and Z018.

Analytical Specificity (Cross Reactivity)

To determine the analytical specificity of **Alere™ i** Strep A 2, 34 commensal and pathogenic microorganisms (33 bacteria and 1 yeast) that may be present in the throat were tested. All of the following microorganisms and yeast produced negative results when tested at a minimum concentration of 2.00 x 10^6 cells/mL of Elution Buffer.

Bacteria	Yeast
Arcanobacterium haemolyticum	*Candida albicans*
Bacillus cereus	
Bordetella pertussis	
Burkholderia cepacia	
Campylobacter rectus	
Corynebacterium diphtheriae	
Enterococcus faecalis	
Escherichia coli	
Fusobacterium necrophorum	
Haemophilus influenzae	
Klebsiella pneumoniae	
Lactobacillus acidophilus	
Moraxella catarrhalis	
Neisseria gonorrhoeae	
Peptostreptococcaceae	
Prevotella oralis	
Pseudomonas aeruginosa	
Staphylococcus aureus	
Staphylococcus epidermidis	
Streptococcus agalactiae	
Streptococcus aginosus	

Bacteria	Yeast
Streptococcus canis	
Streptococcus constellatus **subsp. *pharyngis***	
Streptococcus dysgalactiae **subsp. *equisimilis***	
Streptococcus gallolyticus	
Streptococcus intermedius	
Streptococcus mitis	
Streptococcus mutans	
Streptococcus pneumoniae	
Streptococcus salivarius	
Streptococcus sanguinis	
Treponema denticola	
Veillonella parvula	

In addition, *in silico* analysis was performed to determine whether there is any significant homology between **Alere™ i** Strep A 2 target nucleic acid sequence and the genomes of the following upper respiratory tract microorganisms. None of the organisms maintained genomic sequence that was significantly similar to the **Alere™ i** Strep A 2 target sequences.

Bacteria	Viruses
Candida spp	Adenovirus Type 1
Enterococcus spp.	Adenovirus Type 7
Klebsiella spp.	Human influenza virus A
Lactococcus lactis	Human influenza virus B
Legionella spp.	Human parainfluenza
Mycoplasma pneumoniae	Human metapneumovirus
Pseudomonas spp.	Respiratory syncytial virus Type B
Saccharomyces cerevisiae	Rhinovirus
Stenotrophomonas maltophilia	

Interfering Substances

The following substances, naturally present in throat swab specimens or that may be artificially introduced into the throat, were evaluated with **Alere™ i** Strep A 2 at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Whole Blood	5.0% (v/v)
Mucin	1.0% (w/v)[1]
Human Saliva	5.0% (v/v)[2]
Ibuprofen	20 mg/mL
Acetaminophen	60.4 mg/mL
Acetylsalicylic acid	0.65 mg/mL
Albuterol	0.40 mg/mL
Diphenhydramine HCL	1.0 mg/mL
Cepacol® Sore Throat Lozenges	20% (w/v)
Sucrets® Sore Throat & Cough	20% (w/v)
Halls Plus®	20% (w/v)
ACT® Total Care	20% (v/v)
Cepacol® Mouthwash	20% (v/v)
Listerine® Antiseptic Mouthwash	10% (v/v)[3]
Crest® Complete Multi-Benefit Whitening + Deep Clean Toothpaste	20% (w/v)
Zicam® Oral Mist	20% (v/v)
Chloraseptic® Max Sore Throat Relief + Coating Action	20% (v/v)
Contact Cold & Flu Tablets	20% (w/v)
Robitussin® Maximum Strength Nighttime Cough DM	20% (v/v)
Tylenol® Cold Multi-Symptom Liquid	20% (v/v)
Children's Dimetapp® Cough & Cold	20% (v/v)

[1] 1/3 replicates at 2% w/v mucin produced a false-negative result
[2] 1/3 replicates at 10% v/v saliva produced a false-negative result
[3] 1/3 replicates at 20% v/v Listerine Antiseptic Mouthwash produced a false-positive result

CLIA Waiver Studies:

The same data from the prospective study described in the Performance Characteristics section above were used to determine the accuracy of **Alere™ i** Strep A 2. Testing was performed by operators with no laboratory experience and who are representative of the intended users at CLIA waived testing sites. In this study testing was conducted by 34 intended users at nine (9) study sites that were representative of CLIA waived settings. No training on the use of the test was provided to the operators.

Overall, 981 throat swab specimens were tested with **Alere™ i** Strep A 2, and the results were compared to those of bacterial culture. The performance of **Alere™ i** Strep A 2 for all specimens combined is presented in the clinical study section above. A study was conducted to evaluate the performance of **Alere™ i** Strep A 2 with weakly reactive samples when tested by untrained users. Randomized blind-coded panels, containing negative and low positive (close to the limit of detection {LOD} or assay cutoff) specimens were tested with **Alere™ i** Strep A 2 at 3 sites that were representative of CLIA waived settings (120 tests in total). Six untrained users participated in the study. The testing was conducted over a minimum of 6 days at each site, and was integrated into the users' daily work flow. The performance of **Alere™ i** Strep A 2 in the hands of untrained users with negative samples and samples near the assay cutoff was acceptable, as shown in the table below.

Alere™ i Strep A 2 Testing of Samples near the Assay Cutoff (LOD)

Sample Type	% Detection	95% CI
Strep A Low Positve (C_{95})	98.3% (59/60)	91.1%, 99.7%
True Negative	0% (0/60)	0%, 6.0%

Using risk analysis as a guide, analytical flex studies were conducted on **Alere™ i** Strep A 2. The studies demonstrated that the test is insensitive to stresses of environmental conditions and potential user errors.

SYMBOLS

 Fragile, handle with care	BASE Test Base
CARTRDG Transfer Cartridge	RCVR Sample Receiver
R_x Only Prescription Only (Applies to U.S. only)	

ORDERING AND CONTACT INFORMATION

Reorder numbers:

734-000: Alere™ i Strep A 2 24 Test Kit

734-080: Alere™ i Strep A 2 Control Swab Kit

US + 1 877 441 7440
OUS + 1 321 441 7200

Technical Support Advice Line

Further information can be obtained from your distributor, or by contacting Technical Support on:

US
+ 1 855 731 2288 ts.scr@alere.com

Africa, Russia, CIS
+ 972 8 9429 683 ARCISproductsupport@alere.com

Asia Pacific
+ 61 7 3363 7711 APproductsupport@alere.com

Canada
+ 1 800 818 8335 CANproductsupport@alere.com

Europe & Middle East
+ 44 161 483 9032 EMEproductsupport@alere.com

Latin America
+ 57 2 6618797 LAproductsupport@alere.com

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3. Manual of Clinical Microbiology, 11th Edition, Vol. 1, ASM. (2015) pg. 279.

Alere Scarborough, Inc.
10 Southgate Road
Scarborough, Maine 04074 USA
www.alere.com

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