CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW260004

II. Parent Document Number

K260333

III. CLIA Waiver Type

Dual 510(k) and CLIA Waiver by Application (Dual Submission)

IV. Applicant

Diasorin Molecular, LLC

V. Proprietary and Established Names

LIAISON NES Group A Strep; LIAISON NES Group A Strep Control Swab Kit

VI. Measurand (analyte)

Group A *Streptococcus* (GAS; *Streptococcus pyogenes*) nucleic acid

VII. Sample Type(s)

Direct throat swab

VIII. Type of Test

Qualitative real-time polymerase chain reaction (PCR)

IX. Test System Description

A Overview

The LIAISON NES Group A Strep is a real-time polymerase chain reaction (PCR) based test intended for the qualitative detection of nucleic acid from *Streptococcus pyogenes* (Group A Strep) in direct, freshly collected throat swabs. The system consists of the LIAISON NES instrument, LIAISON NES Group A Strep Cartridge containing all the required PCR reagents, NES Sample Vial containing working solution, and NES Swab for throat sample collection.

For this test, a throat swab sample is collected from a patient and placed into the NES Sample Vial. The swab is snapped at a pre-defined mark, and the sample is released into the working solution. The sample vial contents are squeezed into the LIAISON NES Group A Strep Cartridge. The cartridge is then loaded on the LIAISON NES instrument, a PCR thermocycler, for subsequent automated analysis and result generation. Dye-labeled fluorescent probes and primers amplify and detect conserved regions of GAS bacterial DNA and internal control (IC) DNA, which is used to detect any PCR failures and/or inhibition. At the end of the assay run, qualitative results are reported.

The LIAISON NES Group A Strep Control Swab Kit is provided separately and contains positive and negative external controls intended to be used with the LIAISON NES Group A Strep assay on the LIAISON NES instrument. The Control Swab Kit includes: a negative control swab intended to monitor possible GAS contamination and a positive control swab comprised of lyophilized bacterial cells of *S. pyogenes* (GAS) at a low positive concentration used for a routine check on the system. Quality control result readouts are "Pass" and "Fail".

B Test System Components

The LIAISON NES Group A Strep kit box contains the following:

- (10) Pouched LIAISON NES Group A Strep Cartridges
- (10) NES Swabs for sample collection
- (10) Pouched NES Sample Vials, each containing one foil sealed vial with buffer and one cap
- (1) Printed copy of the Patient Test Quick Reference Guide

Materials required but not provided

- (10) LIAISON NES Group A Strep Positive Control Swab (provided separately as part of the LIAISON NES Group A Strep Control Swab Kit)
- (10) LIAISON NES Group A Strep Negative Control Swab (provided separately as part of the LIAISON NES Group A Strep Control Swab Kit)
- Disposable, powder-free nitrile gloves
- Tongue depressor
- Biohazard waste container
- LIAISON NES instrument

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

The LIAISON NES Group A Strep assay has built-in features that make the test system simple and easy to use with minimal risk of erroneous results. Features that make the system simple to use include:

- The system consists of an instrument, a swab, a sample vial, and a test cartridge. The swab, sample vial, and test cartridge are provided with the assay kit. The cartridge is supplied pre-loaded with the reaction reagents. The user prepares the specimen and loads the cartridge into the instrument. After the user starts the assay via the touchscreen graphical user interface

(GUI), no additional user interaction is required to generate a test result. An additional feature automatically starts the run after 30 seconds once the user has loaded the cartridge into the instrument.

- The assay uses an unprocessed dry throat swab that is placed into a pre-measured buffer in the sample vial.

- The specimen buffer is pre-measured and provided in the sample vial. All other reagents are pre-loaded in the assay cartridge at the time of manufacturing.

- The assay requires only basic specimen manipulation after collection with a dry throat swab, specifically rotating of the swab within the sample vial while squeezing the swab head to release the sample. After rotating the swab within the sample vial, the swab shaft is snapped off at a pre-defined mark on the swab shaft. The sample vial is re-capped and the cap at the end of the sample vial is removed. The sample vial is inserted into the sample port of the cartridge, and the complete contents are squeezed into the cartridge. The user closes the cartridge lid and inserts the loaded cartridge into the instrument.

- The cartridge lid is easily opened and allows easy loading of specimen using the sample vial.

- The cartridge lid provides tactile feedback when the user snaps it shut. Once snapped shut, the cartridge lid is designed to prevent re-opening and prevent additional sample loading.

- No operator action is required to generate a result after the run is started on the instrument.

- The cartridge is designed to allow insertion into the instrument in only one direction/orientation.

- The cartridge has a visual indicator that is automatically detected by a sensor in any instrument, preventing cartridge re-use in the same instrument or in another instrument.

- Technical or specialized training is not required for troubleshooting or interpretation of error codes when using the instrument. When an error is detected, it is assigned to a predefined error code and error message, with suggested mitigation displayed on the graphical user interface (GUI).
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- The instrument has a has a color touchscreen display design for ease of use and facilitates easy-to-read messages.

- There are no maintenance tasks other than routine cleaning of the instrument. The instrument performs self-checks at initialization and between runs. External quality controls in the LIAISON NES Group A Strep Control Swab Kit are also available for the user to check proper functioning of the instrument and are provided separately.

- The instrument incorporates algorithms for processing data that eliminate the need for operator calibration, interpretation, or calculation. The instrument displays results on the graphical user interface (GUI) after completion of the test.

- The system produces a "Positive", "Negative" or "Invalid" result readout for each target in the assay that is displayed on the graphical user interface (GUI). Quality control result readouts are "Pass" and "Fail".

- The test result is automatically displayed upon completion of a run, and the test result report can be printed or saved as a .pdf file. The report is designed to be easy to understand and provides a Test Results summary which includes the operator ID, test date and time, Patient ID, assay name and test type, sample type, cartridge lot, expiry and serial number, instrument serial number, and the software and assay version.

- The supplied Quick Reference Guides and User Manual are written using language appropriate for untrained operators.

B Demonstrating "Insignificant Risk of an Erroneous Result"- Failure Alerts and Fail-Safe Mechanisms

1. Risk Analysis:

   Risk analysis was performed using the Failure Modes and Effects Analysis (FMEA) Method according to ISO 14971 *Medical Devices – Application of risk management to medical devices* and Diasorin's internal risk management process. Potential sources of errors that could adversely affect system performance were identified and mitigated first through system design and then through additional caution in the labeling. All risks of harm to the patient or operator were mitigated to an acceptable level and were supported by flex studies and/or operator instructions.

2. Fail-Safe and Failure Alert Mechanisms:

A. System Controls:

The LIAISON NES Instrument system is designed with numerous fail-safe and failure alert mechanisms to prevent operator and instrument errors as described in **Table 1**.

Table 1. LIAISON NES Instrument System for Fail-Safes and Failure Alert Mechanisms

User Engagement with Assay-Instrument System	Desired/Expected Outcome	Fail-safe and Failure Alert Mechanism(s)
Ambient temperature outside of the instrument specifications (below and above the range limits).	Expected results obtained, or system provides an alert of failure (with cause).	The instrument has a sensor to prevent a test being started if the temperature inside the instrument is outside of the operating range.
Test was stopped before results were obtained.	Error message rendered with cause identified.	The instrument is capable of automatically aborting a test when a critical error is detected.
User turned off the instrument before the test was completed and tried to	Error message rendered with cause identified.	In the event of power loss during a test, the instrument does not allow the user to restart the test upon powering on.

User Engagement with Assay-Instrument System	Desired/Expected Outcome	Fail-safe and Failure Alert Mechanism(s)
resume the test once the instrument was back on.		
Cartridge reaction cuvette foil is broken.	Error message rendered with cause identified.	The system is capable of pressurizing the cuvette. The instrument checks that the cuvette is sealed after filling.
Wrong cartridge is used.	Error message rendered with cause identified.	The cartridge packaging includes a label which displays key information about the cartridge. The instrument allows the user to review a run summary before a test is started. The cartridge packaging label is color-coded to represent the test type.
Incorrect assay definition.	Error message rendered with cause identified.	The cartridge barcode contains the cartridge unique ID, lot, expiration date and test type. The system registers the cartridge assay type via the cartridge barcode upon insertion. The instrument automatically selects the protocol to be run from the assay and specimen input type. The instrument informs the user if an appropriate protocol is not available.
Try to utilize damaged or incomplete barcode	Error message rendered with cause identified.	If the instrument cannot read the cartridge barcode, it informs the user and prevents the run from being performed.
Try to start a test using a cartridge that has already been used.	Provide an error message and/or prevent cartridge loading.	The cartridge has a visual indicator to show that it has not already been used. The system has features to prevent a test being run on the same cartridge more than once.
Move the instrument while the assay is running by tilting the instrument during the test.	Expected results obtained, or system provides an alert of failure (with cause).	Visual indication shown to the user to not move the instrument while running.
Incorrect orientation of cartridge insertion into instrument.	Prevent user from inserting the cartridge in the incorrect orientation.	The cartridge is designed to allow insertion into the instrument in only one direction/orientation.
The altitude of the instrument is above specifications (above the range limits).	Expected results obtained, or system provides an alert of failure (with cause).	The instrument has a sensor to prevent a test being started if the atmospheric pressure inside the instrument is outside of the operating range.
The door is forced opened during a run, exposing internal machinery to the user	Internal machinery is halted. Error message rendered with cause identified.	The instrument has a sensor to detect the open/closed state of the door. If the door is detected as ‘open’ during an assay run, it halts the operation of motors and heaters, aborting the test.
Try to start a test using a cartridge that has expired.	Provide an error message and/or prevent the test from starting.	The cartridge has the expiration date embedded into the instrument-readable QR code. The system has a feature to

User Engagement with Assay-Instrument System	Desired/Expected Outcome	Fail-safe and Failure Alert Mechanism(s)
		check the expiration date of the cartridge and prevent a test being started with an expired cartridge.
Wrong QC sample is used.	Error message rendered with cause identified.	The positive and negative QC packaging includes a label which displays key information about the controls, and an instrument-readable QR code. The system has a feature to check the QC sample type and prevent a test being started with an incorrect QC sample.
Try to start a QC test using a QC sample that has expired.	Provide an error message and/or prevent the test from starting.	The QC sample has the expiration date embedded into the instrument-readable QR code. The system has a feature to check the expiration date of the QC sample and prevent a test being started with an expired sample.

B. Built-in Procedural (Internal) Controls

The LIAISON NES Group A Strep assay includes an internal control (IC) intended to indicate that the test is functioning as expected and to detect any PCR failures and/or inhibition. The assay cartridge contains dye-labeled fluorescent probes and primers to amplify and detect IC DNA (*Arabidopsis thaliana* template DNA). The dye-labeled fluorescent probe of internal control is detected on a separate channel than the *S. pyogenes* (GAS) target. Detection of the IC DNA is required for valid result generation in the absence of a positive ("Positive") call. An "Invalid" result indicates the inability to conclusively determine the presence or absence of *S. pyogenes* DNA in the sample and the inability to conclusively detect the presence of the IC. A new sample must be acquired and tested.

C. External Controls

External controls are provided separately in the LIAISON NES Group A Strep Control Swab Kit containing ten (10) LIAISON NES Group A Strep Positive Control Swabs and ten (10) LIAISON NES Group A Strep Negative Control Swabs. The LIAISON NES Group A Strep Positive Control Swab is a single-use swab (the same swab type as used for sample collection) coated with lyophilized, inactive GAS at a low positive concentration. The positive control mimics the intended specimen and confirms that the bacterial lysis and amplification reaction occur as expected during an assay run. The LIAISON NES Group A Strep Negative Control Swab is a single-use swab (the same swab type as used for sample collection) without sample or matrix. The negative control swab is intended to monitor for possible GAS contamination. The device instructions for use recommend that positive and negative external controls are tested when receiving a new lot of reagents or when a new operator uses the test before proceeding with patient sample testing to ensure the test is functioning as expected and the assay procedure is performed correctly. Control swabs are ready for use without any preparation and are tested following the same procedure used for patient samples.

3. Flex Studies:

Flex studies were conducted to evaluate the performance of LIAISON NES Group A Strep assay and the LIAISON NES Group A Strep Control Swab Kit. Variations in workflow and operating environment that may reasonably be expected to occur with untrained operators in the intended use CLIA-waived setting were evaluated. Test conditions were designed based on risk analyses that considered the complete test system.

Flex studies were conducted by using contrived positive samples of 2 × LoD *S. pyogenes* M3 (ATCC BAA-595) in simulated negative matrix spiked on dry swab and negative samples of simulated negative matrix spiked on dry swab. Testing was conducted according to the Instructions for Use (IFU) for the assay and the Control Swab Kit. Comparative controls were carried out under conditions consistent with use of the device according to its labeling.

The recommended test conditions as described in the device labeling were used as procedural controls to compare with the flex conditions. A negative result was considered in agreement when a negative sample resulted "Negative" on the LIAISON NES Group A Strep assay with a valid Internal control result while a positive result was considered in agreement when a positive sample resulted "Positive".

At the beginning of each testing day, negative and positive external controls were tested on each test instrument. All external controls performed as expected.

The following flex conditions were evaluated using the contrived positive and negative samples.

1) Cartridge Sunlight Exposure
2) Incorrect Sample Storage
3) Incorrect Sample Volume
4) Incorrect Kit Storage
5) Incorrect Control Kit Storage
6) Inadequate Sample Mixing
7) Hold Time Post Sample Addition (Cartridge)
8) Hold Time Post Sample Processing (Sample Vial)
9) Incorrect Workflow
10) Delay in Sample Testing
11) Incorrect Reagent Storage (Cartridge Open Pouch)
12) Incorrect Control Swab Storage (Open Pouch)
13) Barometric Pressure, Temperature and Humidity
14) Extreme Temperature

Flex Study 1: Cartridge Sunlight Exposure

This study was conducted to evaluate the effects of sunlight exposure on the performance of the LIAISON NES Group A Strep assay. The LIAISON NES Group A Strep Cartridge was removed from the protective desiccated foil pouch and exposed to sunlight for 30 minutes, 2 hours or 4 hours before testing. Five (5) negative and five (5) positive samples were tested immediately after cartridge removal from the pouch (without exposing the cartridge to

sunlight) and at each timepoint. Results are shown in **Table 2**. All results were 100% in agreement with expected results.

Table 2. Summary Results for Sunlight Exposure Flex Study

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: no sunlight exposure	0	5/5	5/5
30 minutes of sunlight exposure	0	5/5	5/5
2 hours of sunlight exposure	0	5/5	5/5
4 hours of sunlight exposure	0	5/5	5/5

The results demonstrate that there is an insignificant risk of incorrect results when the cartridge is exposed to direct sunlight for an extended period of time before use. The device labeling provides instructions to keep the test device away from exposure to sunlight.

Flex Study 2: Incorrect Sample Storage

This study was conducted to evaluate the effect of storage of samples at 2-8°C on the LIAISON NES Group A Strep assay. Negative and positive samples were spiked onto NES swabs and stored at 2-8°C for 4 hours and 24 hours. Five (5) negative and five (5) positive samples were tested fresh (immediately after preparation) and at each timepoint. Results are shown in **Table 3**. All results were 100% in agreement with expected results.

Table 3. Summary of Results for Incorrect Sample Storage

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: immediate testing	0	5/5	5/5
2-8°C for 4 hours	0	5/5	5/5
2-8°C for 24 hours	0	5/5	5/5

The results demonstrate that storage of samples at 2-8°C for up to twenty-four (24) hours does not impact performance of LIAISON NES Group A Strep assay. The product Quick Reference Guide (QRG) and Instructions for Use (IFU) both provide instructions to test freshly collected samples and to keep the samples inside the swab tube at room temperature and must be processed within 2 hours from collection.

Flex Study 3: Incorrect Sample Volume

This study was conducted to evaluate the effect of an incorrect sample volume on the performance of the LIAISON NES Group A Strep assay. Sample volumes of 250 µL, 150 µL, 100 µL were tested, which are less than the nominal volume contained within the NES Sample Vial (approximately 700µL). Five (5) negative and five (5) positive sample inputs were tested using the entire sample volume in the NES Sample Vial and each lower volume. Results are shown in **Table 4**. All results were 100% in agreement with expected results for volumes ≥150 µL.

Table 4. Summary of Results for Incorrect Sample Volume

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: entire NES Sample Vial (approx. 700 µL)	0	5/5	5/5
250 µL	0	5/5	5/5
150 µL	0	5/5	5/5

Test Case	Invalid Results	Negative Agreement	Positive Agreement
100 µL	5	1/5	3/5

When less than 150 µl sample volume is used, there is a higher risk of incorrect results (invalids) indicating that squeezing an adequate sample volume into the LIAISON NES Group A Strep Cartridge is necessary to ensure a reliable result. Therefore, the product Quick Reference Guide (QRG) and Instructions for Use (IFU) both bear a warning that failure to transfer all the liquid from the sample vial into the cartridge can cause invalid results.

Flex Study 4: Incorrect Kit Storage

This study was conducted to evaluate the effect of incorrect kit storage conditions on the performance of LIAISON NES Group A Strep kit. The LIAISON NES Group A Strep kit components (LIAISON NES Group A Strep Cartridge, NES Swab Tube and NES Sample Vial) were stored at -20°C (freezer), 2-8°C (refrigerator), and 50°C / 50% RH (incubator) for 3 and 5 days before testing. Five (5) negative and five (5) positive samples were tested after storage according to the device labeling (i.e., at 15-30°C) and with each storage condition. Results are shown in **Table 5**. All results were 100% in agreement with expected results.

Table 5. Summary Results for Incorrect Kit Storage

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: 15-30°C	0	5/5	5/5
-20°C (Freezer) for 3 days	0	5/5	5/5
-20°C (Freezer) for 5 days	0	5/5	5/5
2-8°C (Refrigerator) for 3 days	0	5/5	5/5
2-8°C (Refrigerator) for 3 days	0	5/5	5/5
50°C / 50% RH (Incubator) for 3 days	0	5/5	5/5
50°C / 50% RH (Incubator) for 3 days	0	5/5	5/5

The study results demonstrate that freezing (-20°C), refrigeration (2-8°C) or incubation (50°C / 50% RH) of the LIAISON NES Group A Strep kit components do not compromise the assay performance; all components maintained functionality and performance under these storage conditions after both short-term (3 days) and extended exposure (up to 5 days). The device labeling indicates test kits should be stored at room temperature (15-30°C).

Flex Study 5: Incorrect Control Kit Storage

This study was conducted to evaluate the effects of incorrect storage conditions on the performance of the LIAISON NES Group A Strep Control Swab Kit when used with the LIAISON NES Group A Strep assay. The LIAISON NES Group A Strep Positive Control Swab and LIAISON NES Group A Strep Negative Control Swab were stored at -20°C (freezer), 2-8°C (refrigerator), and 50°C / 50% RH (incubator) for 3 and 5 days before testing. For comparative control testing, positive and negative control swabs stored in accordance with product labeling (i.e., 15-30°C) were tested. Five (5) negative controls and five (5) positive controls were tested with each storage condition. Results are shown in **Table 6**. provides the results agreement for negative and positive samples for all test cases. All results were 100% in agreement with expected results.

Table 6. Summary Result for Incorrect Control Kit Storage

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: 15-30°C	0	5/5	5/5
-20°C (Freezer) for 3 days	0	5/5	5/5
-20°C (Freezer) for 5 days	0	5/5	5/5
2-8°C (Refrigerator) for 3 days	0	5/5	5/5
2-8°C (Refrigerator) for 3 days	0	5/5	5/5
50°C / 50% RH (Incubator) for 3 days	0	5/5	5/5
50°C / 50% RH (Incubator) for 3 days	0	5/5	5/5

The results demonstrated that the incorrect storage of the LIAISON NES Group A Strep Control Swab Kit at -20°C or 2-8°C or 50°C / 50% RH up to five (5) days does not impact the performance of the control swab kit. The device labeling indicates control test kit should be stored at room temperature (15-30°C).

Flex Study 6: Inadequate Sample Mixing

This study was conducted to evaluate the effect of inadequate sample mixing on the performance of LIAISON NES Group A Strep assay. Samples were prepared by modifying the number of times the swab is rotated in the NES Sample Vial while squeezing the swab head and by dipping the swab into the NES Sample Vial instead of squeezing the swab head and rotating the swab in the NES Sample Vial.

Five (5) negative and five (5) positive samples were tested according to the device labeling (control, inserting the swab to the bottom of the NES Sample Vial and the swab head was squeezed while rotating the swab ten (10) times) and for each sample mixing condition. Results are shown in **Table 7**. provides the results agreement for negative and positive samples for all test cases. All results were 100% in agreement with expected results except for the condition in which the swab was dipped into the NES sample vial three (3) times without squeezing or rotating.

Table 7. Summary Results for Inadequate Sample Mixing

Description	Invalid Results	Negative Agreement	Positive Agreement
Control: Squeezing and 10 × swab rotating into NES Sample Vial	0	5/5	5/5
Squeezing and 3 × swab rotating into NES Sample Vial	0	5/5	5/5
0 × swab squeezing or rotating into NES Sample Vial (no squeeze and no rotation)	0	5/5	5/5
3 × swab dip into NES Sample Vial without squeezing or rotating	0	5/5	9/10[†]
10 × swab dip into NES Sample Vial without squeezing or rotating	0	5/5	5/5
10 × swab rotating into NES Sample Vial without squeezing	0	5/5	5/5
3x swab rotating into NES Sample Vial (NES1502) without squeezing	0	5/5	5/5

† One positive replicate for Test conditions 1C resulted in a false negative. Therefore, an additional five (5) replicates were tested.

The results demonstrate that inadequate mixing does not significantly impact performance of LIAISON NES Group A Strep assay. Dipping the swab three (3) times into the sample vial without squeezing or rotating was not sufficient to transfer the sample into the fluid, indicating a risk for erroneous results when squeezing or rotation is not performed.

Therefore, there is a low risk of false negatives if the Instructions for Use are not followed regarding the requirement to squeeze the swab while rotating. This risk of false negatives is reduced in multiple ways. The device labeling recommends that QC testing is performed when adding a new user to the system. At minimum, two control runs (positive and negative) are completed on the system before running patient samples. This enables users to gain competence in the workflow during their initial use of the product, thereby reducing the risk of erroneous results. In addition, the product Quick Reference Guide (QRG) has bolded the "10 times" rotation requirement as well as the word "squeezing" when describing specimen processing and extraction. These instructions are also represented pictorially in the QRG, with red arrows emphasizing rotation of the swab 10 × while squeezing the sample vial. The test procedure in the IFU contains the same written instructions for preparation of the specimen prior to dispensing the specimen into the LIAISON NES Group A Strep Cartridge for testing.

Flex Study 7: Hold Time Post Sample Addition (Cartridge)

This study was conducted to evaluate the effect of storing processed samples in the LIAISON NES Group A Strep Cartridge prior to testing with the LIAISON NES Group A Strep assay. Five (5) negative and five (5) positive and negative swab samples were prepared, processed in the NES Sample Vial, transferred to the NES Group A Strep Cartridge, and then stored inside the cartridge for 0 (control), 120 and 150 minutes at room temperature (15-30°C) before testing. Results are shown in **Table 8.** provides the results agreement for negative and positive samples for all test cases. All results were 100% in agreement with expected results.

Table 8. Summary Results for Hold Time Post Sample Addition (Cartridge)

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: no storage	0	5/5	5/5
120 minutes inside the cartridge at room temperature	0	5/5	5/5
150 minutes inside the cartridge at room temperature	0	5/5	5/5

The results demonstrated that retaining the processed sample within the LIAISON NES Group A Strep Cartridge for up to 150 minutes does not affect the accuracy of LIAISON NES Group A Strep assay. The device labeling describes stepwise procedures to load the cartridge into the instrument. This study supports the device performance in the recommended testing procedures of the assay.

Flex Study 8: Hold Time Post Sample Processing (Sample Vial)

This study was conducted to evaluate the effect of storing processed samples on the performance of the LIAISON NES Group A Strep assay. Five (5) negative and five (5) positive and negative swab samples were be prepared, processed in the NES Sample Vial, and then stored inside the vial for 0 (control), 120 and 150 minutes at room temperature (15 – 30°C) before testing. Results are provided in **Table 9**. All results were 100% in agreement with expected results.

Table 9. Summary Results for Hold Time Post Sample Processing (Sample Vial)

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: no storage	0	5/5	5/5
Sample stored for 120 minutes inside the sample vial at room temperature	0	5/5	5/5
Sample stored for 150 minutes inside the sample vial at room temperature	0	5/5	5/5

The results demonstrated that retaining the processed sample within the NES Sample Vial for up to 150 minutes does not affect the performance of LIAISON NES Group A Strep assay. The device labeling describes stepwise procedures to load the processed sample into the cartridge. This study supports the device performance in the recommended testing procedures of the assay.

Flex Study 9: Incorrect Workflow

This study was conducted to evaluate the effect of performing an incorrect workflow (incorrect sequence of steps) on the performance of LIAISON NES Group A Strep assay. Five (5) negative and five (5) positive samples were tested using the workflow described in the device labeling (control) and the following conditions: (1) correct sample swab processing in the NES Sample Vial except for incorrect disposal of the swab prior to dispensing the sample into the cartridge and (2) the incorrect addition of the contents of the NES Sample Vial into the cartridge first, then swirling the swab ten times in the cartridge, followed by disposal of the swab. Results are shown in **Table 10**. provides the results agreement for negative and positive sample inputs for all test cases. All results were 100% in agreement with expected results.

Table 10. Summary Results for Incorrect Workflow

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: Correct sample processing and dispensing the sample into the cartridge	0	5/5	5/5
Swab correctly processed in the sample vial but disposed before dispensing the sample contents into the cartridge	0	5/5	5/5
Sample vial content added to the cartridge first, followed by swab rotated 10x in the cartridge and disposed	0	5/5	5/5

Both incorrect sample processing methods of discarding the swab (incorrectly) from the sample vial before dispensing the liquid into the cartridge, and the method of first dispensing the liquid into the cartridge (incorrectly), then inserting the swab to be tested, rotating 10×, and subsequently discarding the swab, did not impact the performance of LIAISON NES Group A Strep assay. The results demonstrate that there is an insignificant risk of incorrect results when the test operator performs an incorrect sequence of steps to prepare and test the sample. The device labeling describes stepwise procedures to process the swab and transfer the sample into the cartridge.

Flex Study 10: Delay in Sample Testing

This study was conducted to evaluate the effect of a delay in sample testing on the performance of the LIAISON NES Group A Strep assay. Five (5) negative and five (5) positive spiked swab samples were processed and tested immediately after preparation (control) or the spiked swabs were stored in NES Swab Tubes at different environmental conditions for different time points (representing incorrect sample storage duration) before testing. Results are shown in **Table 11**. All results were 100% in agreement with expected results.

Table 11. Summary Results for Delay in Sample Testing

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: immediate testing	0	20/20	20/20
2 hours at 15°C and 30% RH	0	5/5	5/5
4 hours at 15°C and 30% RH	0	5/5	5/5
2 hours at 15°C and 80% RH	0	5/5	5/5
4 hours at 15°C and 80% RH	0	5/5	5/5
2 hours at 32°C and 30% RH	0	5/5	5/5
4 hours at 32°C and 30% RH	0	5/5	5/5
2 hours at 32°C and 80% RH	0	5/5	5/5
4 hours at 32°C and 80% RH	0	5/5	5/5

The results demonstrate that a delay in testing samples stored in the swab tube for up to four (4) hours at varied environmental conditions up to 32°C and 80% RH did not affect the performance of LIAISON NES Group A Strep assay. The results demonstrate that there is an insignificant risk of incorrect results when the test operator does not follow product instructions and stores the collected sample in the swab tube for an extended period under extreme environmental conditions before testing. The device labeling describes stepwise procedures to process the spiked swabs, and this study supports the performance in the expected operating environment of the device.

Flex Study 11: Incorrect Reagent Storage (Cartridge Open Pouch)

This study was conducted to evaluate the effect of incorrect reagent storage (cartridge open pouch) on performance of the LIAISON NES Group A Strep assay. Five (5) negative and five (5) positive samples were tested with LIAISON NES Group A Strep cartridges immediately after removing them from their protective foil pouches (control) and with LIAISON NES Group A Strep cartridges that were opened and stored in different environmental conditions

for various periods of time. Results are shown in **Table 12**. All results were 100% in agreement with expected results.

Table 12. Summary Result for Incorrect Reagent Storage (Cartridge Open Pouch)

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: immediate testing	0	20/20	20/20
2 hours at 15°C and 30% RH	0	5/5	5/5
4 hours at 15°C and 30% RH	0	5/5	5/5
24 hours at 15°C and 30% RH	0	5/5	5/5
2 hours at 15°C and 80% RH	0	5/5	5/5
4 hours at 15°C and 80% RH	0	5/5	5/5
24 hours at 15°C and 80% RH	0	5/5	5/5
2 hours at 32°C and 30% RH	0	5/5	5/5
4 hours at 32°C and 30% RH	0	5/5	5/5
24 hours at 32°C and 30% RH	0	5/5	5/5
2 hours at 32°C and 80% RH	0	5/5	5/5
4 hours at 32°C and 80% RH	0	5/5	5/5
24 hours at 32°C and 80% RH	0	5/5	5/5

The study demonstrated that storage of open pouch LIAISON NES Group A Strep Cartridge in varied environmental conditions for up to 24 hours did not have an adverse effect on the performance of the LIAISON NES Group A Strep assay. The device labeling describes stepwise procedures after opening the cartridge pouch, and this study supports the performance in the expected operating environmental conditions of the device. .

Flex Study 12: Incorrect Control Swab Storage (Open Pouch)

This study was conducted to evaluate the effect of incorrect storage conditions (swab open pouch) on the performance of the LIAISON NES Group A Strep Control Swab Kit when used with the LIAISON NES Group A Strep assay. Five (5) LIAISON NES Group A Strep Negative Control Swabs and five (5) LIAISON NES Group A Strep Positive Control Swabs were tested immediately after removal from their protective pouches (control) and after storage in different environmental conditions for various periods of time. Results are shown in **Table 13**. All results were 100% in agreement with expected results.

Table 13. Summary Result for Incorrect Control Swab Storage (Open Pouch)

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: immediate testing	0	20/20	20/20
Storage for 2 hours at 15°C and 30% RH	0	5/5	5/5
Storage for 4 hours at 15°C and 30% RH	0	5/5	5/5
Storage for 24 hours at 15°C and 30% RH	0	5/5	5/5
Storage for 2 hours at 15°C and 80% RH	0	5/5	5/5
Storage for 4 hours at 15°C and 80% RH	0	5/5	5/5
Storage for 24 hours at	0	5/5	5/5

Test Case	Invalid Results	Negative Agreement	Positive Agreement
15°C and 80% RH			
Storage for 2 hours at 32°C and 30% RH	0	5/5	5/5
Storage for 4 hours at 32°C and 30% RH	0	5/5	5/5
Storage for 24 hours at 32°C and 30% RH	0	5/5	5/5
Storage for 2 hours at 32°C and 80% RH	0	5/5	5/5
Storage for 4 hours at 32°C and 80% RH	0	5/5	5/5
Storage for 24 hours at 32°C and 80% RH	0	5/5	5/5

The results demonstrated that the storage of LIAISON NES Group A Strep Positive Control Swab and LIAISON NES Group A Strep Negative Control Swab in varied environmental conditions for up to 24 hours did not have an adverse effect on results. The device labeling indicates not to open the pouch until ready to use and perform the test immediately after preparing the cartridge.

Flex Study 13: Barometric Pressure, Temperature and Humidity

This study was conducted to evaluate the effect of extreme temperature, humidity and barometric pressure conditions on the functionality and performance of the LIAISON NES Group A Strep assay as well as the LIAISON NES instrument. Five (5) negative and five (5) positive samples were tested for each condition. Results are shown in **Table 14**. All results were 100% in agreement with expected results, with the exception of testing with a climatic chamber setting at 6889 ft and 22°C.

Table 14. Summary Results for Barometric Pressure, Temperature and Humidity

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: 22°C with 50% RH	0	5/5	5/5
Execution with climatic chamber settings at 15°C with 80% RH	0	5/5	5/5
Execution with climatic chamber settings at 32°C with 80% RH	0	5/5	5/5
Execution with climatic chamber setting at 6889 ft (2100 m) at 22°C	NA†	NA†	NA†
Execution with climatic chamber setting >6561 (2000 m) and < 6889 (2100 m) ft at 22°C	0	5/5	5/5
Execution with climatic chamber settings at 6561 ft (2000 m) at 22°C	0	5/5	5/5

NA† Tests results were not available at this altitude as the condition did not allow to test.

The study results demonstrated that extremes in temperature and humidity do not impact the accuracy of results. Regarding altitude, it was not possible to perform the test at extreme barometric pressure (6889 ft (2100 m) at 22°C), whereas the instruments were able to start and complete a run at 6594 ft (2010 m) at 22°C , and at 6561 ft (2000 m) at 22°C. This supports an operating altitude up to 2000 m. The instrument labeling indicates an operating altitude up to 2000 m.

Flex Study 14: Extreme Temperature Additional Flex Study

This study was conducted to evaluate the effect of extreme temperature conditions on the functionality and performance of the LIAISON NES Group A Strep assay as well as the LIAISON NES instruments. Five (5) negative and five (5) positive samples were tested for each condition. Results are shown in **Table 15**. All results were in agreement with expected results.

Table 15. Summary Results Extreme Temperature Additional Flex Study

Test Case	Invalid Results	Negative Agreement	Positive Agreement
Control: 22°C	0	5/5	5/5
Climatic chamber setting at 5°C	0	5/5	5/5
Climatic chamber setting at 10°C	0	5/5	5/5
Climatic chamber setting at 35°C	0	5/5	5/5
Climatic chamber setting at 40°C	0	5/5	9/10†

† One positive replicate tested for condition 40°C resulted in an instrumental error. Therefore, an additional five (5) replicates were tested.

This study provided expected results across temperatures ranging from 5°C to 35°C, demonstrating that this temperature range does not affect result accuracy, with testing showing 100% agreement for both low positive and negative samples. Based on the results of this testing, there is an insignificant risk of erroneous result reporting when performing the test at operating temperatures ranging from 5°C to 35°C. The device labeling indicates to store and test the assay at room temperature (15 to 30°C).

C Demonstrating "Insignificant Risk of an Erroneous Result" - Accuracy

1. Comparison Study

a. Study Design

The objective of the clinical study was to evaluate the performance of LIAISON NES Group A Strep assay in the hands of the intended users when performed in a CLIA-waived setting.

i. Study Sites and Duration

The performance of the LIAISON NES Group A Strep assay in the hands of untrained users was evaluated in a prospective clinical study that was performed at four geographically diverse clinical sites within the United States. All four sites followed the same protocol and procedures, were subject to the same monitoring process, and were considered representative of CLIA-Waived intended use sites. The sites included two pediatric outpatients, one primary clinic for urgent care and occupational medicine and one primary clinic for urgent care, specialty care, pediatrics and family medicine.

Specimen collection began in April 2025 and concluded in December 2025.

Specimens were collected prospectively under informed consent. Reference culture testing was performed at one external reference site and testing was started within 72 hours of collection for all specimens.

ii. Operators

A total of 10 operators participated in the prospective clinical study, which was conducted at four sites and included two or three operators per site. The participating operators were selected from among site staff and represented a diverse range of educational backgrounds and work experience who were considered representative of untrained operators. No operators had prior clinical laboratory testing experience. No hands-on training regarding the LIAISON NES Group A Strep assay or LIAISON NES instrument was provided to operators, who were only provided with the LIAISON NES Instrument User Manual and the LIAISON NES Group A Strep Instructions for Use (IFU) and Quick Reference Guides (QRG). All operators completed a questionnaire after testing.

The summary of samples tested in this clinical study stratified by site and operators are shown in **Table16**.

Table 16. Summary of samples tested in the clinical study stratified by site and operator

Site	Operator #	Samples Tested [a]	LIAISON NES Group A Strep Result			
			Positives	% Positive	Invalids	% Invalid
01	1	205	23	11.2 %	5	2.4 %
	2	125	10	8.0 %	2	1.6 %
	3	7	1	14.3 %	0	0.0 %
	Subtotal	**337**	**34**	**10.1 %**	**7**	**2.1 %**
02	1	202	33	16.3 %	4	2.0 %
	2	176	24	13.6 %	0	0.0 %
	3	61	12	19.7 %	1	1.6 %
	Subtotal	**439**	**69**	**15.7 %**	**5**	**1.1 %**
03	1	204	20	9.8 %	4	2.0 %
	2	180	12	6.7 %	1	0.6 %
	Subtotal	**384**	**32**	**8.3 %**	**5**	**1.3 %**
04	1	149	12	8.1 %	3	2.0 %
	2	93	10	10.8 %	2	2.2 %
	Subtotal	**242**	**22**	**9.1 %**	**5**	**2.1 %**
Total		**1402**	**157**	**11.2 %**	**22**	**1.6 %**

iii. Instructions for Use

Operators who participated in evaluating the clinical performance of the LIAISON NES Group A Strep assay received no training on how to install and set up the instrument or perform the assay. They were instructed to refer solely to the Instructions for Use (IFU) and Quick Reference Guide (QRG) for running quality control tests and testing patient specimens.

iv. Subjects (Patients) and Specimens

The prospective clinical study included specimens that were collected under informed consent. Patient specimens that met the following characteristics were eligible for inclusion in the study:

(1) Specimen is from patient with active signs and symptoms of pharyngitis, including sore throat, difficulty or pain with swallowing, anterior cervical lymphadenopathy, palatal petechiae, pharyngeal and tonsillar erythema, tonsillar hypertrophy with or without exudates, etc., at time of collection.
(2) Patient consents to participate in the study

Patient specimens with any one of the following characteristics were not eligible for inclusion in the study:

(1) Incorrect swab type
(2) Specimen stored in transport media (no transport media should be used with the device)
(3) Incorrect specimen handling (e.g. specimens not stored at recommended temperature)
(4) Specimen is from a patient that does not provide informed consent or withdraws informed consent
(5) Specimen is from a patient that has received antibiotics treatment up to 14 days prior to specimen collection

A total of 1423 unique specimens that met the pre-determined inclusion criteria were prospectively collected across four geographically diverse US sites and enrolled in the study. The collection of samples from each enrolled patient included two (2) swabs: one dry throat swab for testing directly with the LIAISON NES Group A Strep assay and another throat swab placed in 1 mL Copan liquid amies for reference testing. Both specimens (the dry throat swab for LIAISON NES Group A Strep assay and the throat swab placed in 1mL Copan liquid amies) were collected concurrently by a healthcare professional.

Clinical sample testing using the LIAISON NES Group A Strep assay was performed by untrained operators at all four collection sites. Out of the 1423 specimens enrolled in the prospective arm of the study, 21 (1.5%) specimens were disqualified and removed from further analysis as summarized in **Table 17**.

Table 17. Summary of Excluded Specimens

Reason for exclusion	Site 01	Site 02	Site 03	Site 04	Total
Total specimens enrolled in the study	338	451	385	249	1423
Inability to verify time window	0	3	0	0	3
Indeterminate reference result	1	0	0	0	1
Reference lab received sample >72hrs post-collection	0	5	1	7	13
Reference swab mislabeled	0	4	0	0	4
Total specimens excluded from the study	1	12	1	7	21
Total specimens included in the study	337	439	384	242	1402

b. Results and Analysis

Estimates of sensitivity, specificity, and negative predictive value (NPV) for the prospective clinical data set were calculated to demonstrate the performance of the LIAISON NES Group A Strep assay compared to the reference method. Discordant analysis using three FDA-cleared molecular assays was performed when the LIAISON NES Group A Strep results were not in agreement with the reference assay results. The results from discordant analysis are included as footnotes to the performance table and were not used to alter performance calculations.

Of the 1402 clinical specimens included in the prospective study analysis, 1380 (98.4%) generated valid LIAISON NES Group A Strep results upon testing. Repeat testing was not performed.

The overall performance of the LIAISON NES Group A Strep assay when compared to reference culture method is summarized in Table 18A (all sites combined) and 18 B (stratified by sites).

Table 18 A. CLIA Clinical Performance of LIAISON NES Group A Strep

All sites combined		Reference Culture Method		
		Positive	**Negative**	**Total**
LIAISON NES Group A Strep	**Positive**	104	53†	157
	Negative	0	1223	1223
	Total	104	1276	1380

Sensitivity	100% (104/104)	95% CI (96.44% - 100%)
Specificity	95.85% (1223/1276)	95% CI (94.61% - 96.81%)
PPV	66.24% (104/157)	95% CI (58.54% - 73.17%)
NPV	100% (1223/1223)	95% CI (99.69% - 100%)

† Discordant result analysis showed that Strep A was detected in 51/53 False Positive specimens by at least one of three FDA-cleared molecular assays.

Table 18 B. Performance of the LIAISON NES Group A Strep Stratified by Site

Site	Total	TP	FN	TN	FP	Sensitivity [95% CI]	Specificity [95% CI]
Site 1	330	21	0	296	13	100% (21/21) [84.54% - 100%]	95.79% (296/309) [92.94% - 97.53%]
Site 2	434	50	0	365	19	100% (50/50) [92.86% - 100%]	95.05% (365/384) [92.40% - 96.81%]
Site 3	379	20	0	347	12	100% (20/20) [83.89% - 100%]	96.66% (347/359) [94.25% - 98.08%]
Site 4	237	13	0	215	9	100% (13/13) [77.19% - 100%]	95.98% (215/224) [92.54% - 97.87%]
All Sites	1380	104	0	1223	53	100% (104/104) [96.44% - 100%]	95.85% (1223/1276) [94.61% - 96.81%]

TP = true positive, FN = false negative, TN = true negative, FP = false positive, CI = confidence interval

The LIAISON NES Group A Strep demonstrated overall acceptable performance, with sensitivity of 100% [95% CI = 96.4 – 100%] and specificity of 95.85% [95% CI = 94.6 – 96.8%] when compared to the reference culture method. The clinical performance provided was acceptable to support use of the LIAISON NES Group A Strep in CLIA Waived environments.

2. Device Performance with Analyte Concentrations Near the Cutoff

A reproducibility study was conducted to evaluate the performance of the LIAISON NES Group A Strep assay with weakly reactive samples when testing was performed by untrained users. A panel of contrived throat swabs was tested at three CLIA-waived sites by a total of six untrained operators (two operators at each site). Contrived positive samples were prepared using two strains of *Streptococcus pyogenes* M1 (ATCC 700294) and M3 (ATCC BAA-595) in simulated negative throat sample matrix. Each strain was spiked onto dry swabs at two different concentrations relative to the limit of detection (LoD) for each strain: low positive (LP, ~1 × LoD) and moderate positive (MP, ~3 × LoD). LIAISON NES Group A Strep Positive Control Swabs were also included in the testing panel. Negative samples were prepared by spiking simulated negative throat swab matrix (**Table 19**).

Table 19. Reproducibility Panel Members

Panel Members	Strains	Approximate Concentration
M1 LP	*S. pyogenes* M1 (ATCC 700294)	1 × LoD
M1 MP	*S. pyogenes* M1 (ATCC 700294)	3 × LoD
M3 LP	*S. pyogenes* M3 (ATCC BAA-595)	1 × LoD
M3 MP	*S. pyogenes* M3 (ATCC BAA-595)	3 × LoD
Negative Sample	Simulated Negative Thorat Swab Matrix only	Not applicable
Positive Control	LIAISON NES Group A Strep Positive Control	Not applicable

LP = low positive, MP = moderate positive

Each sample panel member was blinded and tested by two different operators at each of the three CLIA-waived testing sites. Each operator tested each panel member in three replicates each day for a total of five testing days using one lot of LIAISON NES Group A Strep Cartridges and one lot of external controls. A total of ninety (90) replicates (3 replicates × 2 operators × 3 sites × 5 days) were evaluated for each panel member. A total of fourteen LIAISON NES instruments, at least two per site, were used in the evaluation.

Reproducibility results are reported as percent detection: positive/tested × 100% and summarized in Table 20.

Table 20. Reproducibility of LIAISON NES Group A Strep

Sample Type	% Detection (Positive / Tested)				Percent Agreement (95% CI)
	Site 1	Site 2	Site 3	Overall	
M1 Low Positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (95.9% - 100.0%)

Sample Type	% Detection (Positive / Tested)				Percent Agreement (95% CI)
	Site 1	Site 2	Site 3	Overall	
M1 Medium Positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (95.9% - 100.0%)
M3 Low Positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (95.9% - 100.0%)
M3 Medium Positive	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (95.9% - 100.0%)
Negative Sample	0% (0/30)	0% (0/30)	0% (0/30)	0% (0/30)	100% (95.9% - 100.0%)
Positive Control	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (95.9% - 100.0%)

The study results demonstrate that untrained users were able to perform the test correctly and the test provided the expected result for samples near the cutoff.

3. Operator Questionnaire

The 10 operators who participated in the clinical study were confirmed to be representative of typical operators in the intended use environment for near-patient testing and untrained in the use of the LIAISON NES Group A Strep assay. Following completion of the clinical study, each operator completed a post-study questionnaire to assess the ease and the usefulness of the instruction for use (IFU) and Quick Reference Guides (QRG), the ability of operators to follow the instructions for Quality Control testing, and the ease of reading and recording results, and ease of using instrument. The questionnaire contained 17 questions related to ease of use and 8 questions assessing operators' ability to correctly interpret results as displayed on the instrument. Scoring for each question was implemented as follows:

- Yes/No questions were summarized as percentage of "Yes" responses
- Agreement-based responses were converted to numerical scores, with mean scores calculated for each question:
  - Strongly Agree = 5
  - Agree = 4
  - Neutral = 3
  - Disagree = 2
  - Strongly Disagree = 1
- Mean scores were calculated for each question

The results of operators' questionnaire were summarized by site, including individual response scores and the overall score, as shown in **Table 21**.

Additionally, the interpretation of results section of the questionnaire included example screenshots from the LIAISON NES Instrument and asked operators to select multiple-

choice responses that best represented how they would interpret the results. The images included examples of passing and failing Quality Control runs, invalid runs and positive and negative assay results. The overall score for the proficiency portion was 100% (10/10), with all operators correctly interpreting each result.

Table 21. Post-Study Operator Questionnaire Results

Question	Site 1	Site 2	Site 3	Site 4	Overall
The NES instrument was easy to install. [a]	5	4.7	5	4	4.7
The NES instrument was easy to use overall. [a]	5	4.7	5	4	4.7
The NES instrument software was easy to use. [a]	5	4.7	5	4	4.7
Did you read the Quick Reference Guide before the first time you used the instrument? [b]	100%	100%	100%	100%	100%
The Quick Reference Guide was easy to read and understand. [a]	5	4.7	5	4	4.7
Did the Quick Reference Guide provide all the information you needed to successfully set up your NES instrument? [b]	100%	100%	100%	100%	100%
Did you require assistance the first time you used the instrument? [b]	0%	0%	0%	0%	0%
Did you refer back to the Quick Reference Guide after the first time you used the instrument? [b]	33.3%	66.7%	50%	50%	50%
QC testing was easy to run on the NES system. [a]	5	5	5	4	4.8
Did you encounter any technical issues with the NES System? [b]	66.7%	100%	100%	100%	90%
It was easy to troubleshoot issues with the NES system using the documentation provided (manual, QRG, IFU). [a]	4.3	4.3	4	3.5	4.1
It was easy to prepare a sample for testing on the Group A Strep (GAS) assay. [a]	4.7	5	5	4.5	4.8
It was easy to run a test using the Group A Strep (GAS) assay. [a]	5	5	5	4	4.8
Did you read the assay Quick Reference Guide before the first time you ran a test? [b]	100%	100%	100%	100%	100%
Did the assay Quick Reference Guide provide all the information you needed to successfully run a test? [b]	100%	100%	100%	100%	100%
It was easy to see and interpret the test results. [a]	5	5	5	4.5	4.9
Was the documentation provided (manual, QRG and IFU) adequate to perform testing without additional instruction? [b]	100%	100%	100%	100%	100%

[a] Numerical values were assigned and averages are shown (Strongly Agree = 5, Agree = 4, Neutral = 3, Disagree = 2, Strongly Disagree = 1).
[b] Results are presented as percent based on the ratio of answer "Yes" divided by total and multiplying by 100.

The post-study operator questionnaire results demonstrate that the LIAISON NES System and LIAISON NES Group A Strep assay can be used accurately and reliably by intended operators in CLIA-Waived settings following self-training with the IFU and QRG. This study supports that the LIAISON NES Group A Strep assay was easy to use and that the training materials provided (Instrument User Manual, Quick Reference Guides and Instructions for Use) were adequate to perform the test without additional instructions.

D Labeling for Waived Devices

The labeling associated with the LIAISON NES Group A Strep device consists of:

1. LIAISON NES Group A Strep Instructions for Use
2. LIAISON NES Group A Strep Control Swab Kit Instructions for Use

The following elements are present in the labeling:

- The QRG is written at no higher than a 7th grade reading level. It contains illustrations of the device components and procedure steps.
- The package insert and the QRG identify the test as CLIA-waived.
- The package insert contains a statement that a Certificate of Waiver is required to perform the test in a waived setting.
- Per 42 CFR 493.15(e)(1), the package insert contains a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test.
- Instructions for conducting quality control (QC) procedures are integrated with procedural instructions for performing the test in both the package insert and the QRG.
- Appropriate cautions have been added to the package insert and QRI to ensure safe use of the product.
- The results of a Clinical Study that support the determination of eligibility for CLIA Waiver are included in the package insert.
- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

XI. Benefit-Risk Considerations

The overall sensitivity of the LIAISON NES Group A Strep is 100% with the lower bound of the 95% CI of 96.4%, the overall NPV is 100% with the lower bound of the 95% CI of 99.7% at a prevalence of 7.5% encountered in this study. When extrapolated to a prevalence of 30%, the overall NPV is 100%. Samples tested are approximately distributed evenly (17% to 31%) across the testing sites.

Support for the exclusion of culture confirmation of assay-negative GAS results from this assay was assessed using parameters and criteria as previously assessed for K141173. Briefly, the following criteria for sensitivity and negative predictive value (NPV) should be demonstrated to exclude the statement requiring follow-up culture for negative results in the Intended Use for GAS assays:

1) Overall sensitivity ≥98%, with the lower bound of the 95% CI of ≥93% from ≥ 100 positive specimens;
2) Overall NPV ≥99%, with the lower bound of the 95% CI of ≥97% extrapolated based on 30% prevalence (recent studies presented to the FDA indicated that it is unlikely that the prevalence for GAS will exceed 30% during the peak season for GAS pharyngitis);
3) Each testing site demonstrates an NPV of ≥98% and an approximately even distribution of samples is observed among the sites.

Based on these values and the criteria noted above, there is no need to add a statement requiring follow-up culture for negative results in the Intended Use for this assay. The rapid results associated with high specificity offer a benefit to patients in management of a positive Strep A result.

XII. Conclusion

The submitted information in this CLIA waiver application supports a CLIA waiver approval decision.