U.S. FOOD & DRUG ADMINISTRATION

CLIA Waiver by Application Approval Determination
Decision Summary

I. Document Number

CW240005

II. Parent Document Number

K240280

III. CLIA Waiver Type

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

IV. Applicant

Nano-Ditech Corporation

V. Proprietary and Established Names

Nano-Check RSV Test

VI. Measurand (analyte)

Nucleoprotein antigen from Respiratory Syncytial Virus (RSV)

VII. Sample Type(s)

Anterior nasal swab specimens

VIII. Type of Test

Qualitative lateral flow immunoassay

IX. Test System Description

A Overview

The Nano-Check RSV Test is an immunochromatographic lateral flow assay for detection of extracted RSV nucleoprotein antigens in human anterior nasal swab specimens. To initiate testing, a flocked swab is used to collect anterior nasal swab specimens from both nostrils. The patient swab sample is placed into a Reagent Tube containing extraction buffer. The buffer disrupts the virus particles present in the sample, exposing the internal viral nucleoproteins. The

test device is comprised of a plastic cassette containing the test strip and the sample well (Figure 1). After the extraction step, the sample is dispensed into the sample well of the test device.

Figure 1: Test Device of Nano-Check RSV Test

The sample will migrate up the test strip via capillary action. If RSV nucleoprotein antigens are present, they will bind to the colloidal gold particles coupled with monoclonal antibodies specifically targeting the RSV nucleoprotein antigen. The antigen-conjugate immunocomplexes migrate across the test strip and are captured at the test line (T) of the nitrocellulose membrane forming a visible pinkish-red line. Sample continues to flow through the test device which also contains a procedural control line (C) to assess adequate sample flow and functioning of the test device. A visible pinkish-red line at the control line (C) should always appear if the assay is performed correctly. If no visible signal appears on (C) line, the test result is invalid, and this sample should be tested again with another test cassette. Test results are read 15 minutes after the sample is added to the cassette.

External positive control and negative control swabs are provided with each kit of Nano-Check RSV Antigen Tests and are intended to be used as quality control samples to confirm that the reagents are functional and the assay procedure is performed correctly.

B Test System Components

The Nano-Check RSV Test kit contains reagents sufficient to run 20 tests and includes:

- 20 Test devices in sealed aluminum foil pouch with desiccant
- 20 Reagent tubes prefilled with 350 µL extraction buffer containing buffer with detergents, antibiotics and sodium azide
- 20 Dropper tips
- 20 Individually packed sterile nasal swabs
- One Positive Control swab
- One Negative Control swab
- One Instructions for Use (IFU)
- One Quick Reference Instructions (QRI)

X. Specific Contents for CLIA Waiver

A Demonstrating "Simple":

- The test uses anterior nasal swab specimens with minimal processing.
- The test needs only basic, non-technique-dependent specimen manipulation. An untrained operator can conduct the test by performing a few simple steps:
    1. Collect sample using the provided sterile swabs.
    2. Place the swab in the Reagent tube with extraction buffer; mix by rotating.
    3. Attach Dropper tip to the tube.
    4. Dispense two drops from the Reagent tube onto the test device.
    5. Wait 15 minutes.
    6. Visually inspect the test (T) and control (C) lines on the test device to read the result.
- The test requires no calibration.
- The test requires only basic reagent handling to obtain accurate test results. No processing of reagents is needed prior to combining test reagent and sample.
- The provided reagent is premeasured and provided in single-use vials.
- The test device contains a control line which serves as a built-in internal procedural control and gives confirmation of sample addition and proper test execution.
- No pipetting is required; dropper tips for the Reagent tube are provided for adding sample dropwise to the test cartridge.
- The test does not require any operator intervention during the analysis step.
- The results are easy to determine, with clear presence or absence of a line indicating a 'positive' or 'negative.'
- If an invalid result is obtained, the operator is instructed to repeat the test.
- Technical or specialized training is not required for troubleshooting or error code interpretation.
- There are no required electronic or mechanical maintenance tasks.
- The test device is for single use.
- Contains a Quick Reference Instruction sheet that is written in simple language at a 7th grade reading level and includes clear diagrams to guide the user.

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

1. **Risk Analysis**:

   Risk analysis was performed by the sponsor using the Failure Modes and Effects Analysis (FMEA) Method in accordance with *ISO 14971:2012 - Medical Devices - Application of Risk Management to Medical Devices* and Nano-DiTech Corporation's internal procedures. The detailed analysis included potential failure modes and effect of the failure, potential causes, built in control measures and evaluation of severity. The sources of error considered include the intended user, environment, human factors/potential human errors, specimen and reagent integrity.

   Potential sources of errors that could adversely affect test performance were identified and mitigated through system design and cautions in the labeling. The identified risks which could result in erroneous test results were evaluated in flex studies that stressed the functional limits of the test system (see below).

2. **Fail-Safe and Failure Alert Mechanisms:**

The Nano-Check RSV Test is designed with the following failure alert mechanisms intended to reduce the risk of device malfunction and procedural errors when performing the assay.

Built-in Procedural Control
The Nano-Check RSV Test has a built-in internal procedural control which monitors that sufficient volume of the sample is added and the reagent flow across the membrane occurred. Formation of a pinkish-red line in the control region on the strip confirms proper sample application and that the reagents are functioning appropriately. If no visible signal appears on the control line, the test result is invalid, and the operator is instructed in the labelling to test the sample again with another test device.

External Controls
One Positive Control swab and one Negative Control swab are included in each test kit. The users are instructed to run kit controls under the following circumstances:

- Each new operator prior to performing tests on patient samples
- When opening a new test kit lot
- Whenever a new shipment of test kits is received

3. **Flex Studies:**

Based on comprehensive risk analysis, potential failure risks were evaluated in flex studies described below. The test samples used in the flex studies were prepared in clinical matrix (nasal fluid) and consisted of:

- Negative sample: un-spiked nasal fluid
- Weakly Positive sample: RSV A Long strain at 2x LoD (Limit of Detection) or 3.2×10^3 $TCID_{50}$/mL

Except where indicated below, each sample was tested in five replicates, for each condition being evaluated in the flex studies, following the test instructions. Each flex study included testing the samples under control (normal) conditions.

Specimen and Reagent Handling

- *Effect of Temperature on Stability of Specimen Swabs:*
  Specimen stability after collection and prior to testing was assessed at ambient temperature (23.5°C), high room temperature (30°C) and refrigerated (2-8°C), after 1, 2, 4, 8, 24 and 48 hours of storage. Five replicates of each sample were tested at each timepoint for each condition. No false results were observed up to 48 hours at all temperature conditions.

  Labeling of Nano-Check RSV Test instructs the user to process freshly collected nasal samples no later than one hour after specimen collection when kept at room temperature

(l5°C to 30°C) or within 24 hours when stored under refrigerated conditions (2°C to 8°C).

- *Effect of Repeated Freeze-Thawing of Specimen Swab Before Extraction:*

  The Nano-Check RSV Test directions instruct the user to test freshly collected nasal samples within one hour after specimen collection, when kept at room temperature (15°C to 30°C), or within 24 hours when stored under refrigerated conditions (2°C to 8°C). This flex study assessed the stability of specimens that may have been inadvertently frozen prior to testing. The test samples were subjected to three freeze-thaw cycles (24 hours of storage at -20°C, followed by thawing at ambient room temperature). The results showed that Weakly Positive swabs remained stable for one freeze-thaw cycle. However, two or three freeze-thaw cycles resulted in false negative results. No false positive results were observed for up to three freeze-thaw cycles with the Negative swabs. Labeling of Nano-Check RSV Test instructs the user to not freeze the swab specimens before testing.

- *Effect of Nasal Discharge on Specimen Swab Before Extraction:*

  To investigate the impact of substantial nasal discharge on the assay performance, a simulated study was conducted with nasal discharge collected by blowing noses. Ten replicates of Weakly Positive swabs (coated with the extra nasal discharge) and Negative swabs (not coated with the nasal discharge) were tested with Nano-Check RSV Test. All positive and negative samples produced expected results for all testing conditions demonstrating that the risk of erroneous results from heavy nasal discharge is minimal.

- *Effect of Temperature on Nano-Check RSV Test Storage Stability:*

  This study evaluated the effect of using unopened Nano-Check RSV Tests stored outside the specified temperature of 2°C-30°C. The Nano-Check RSV Test kit including the test device, Reagent tube, and Negative and Positive Control swabs, were placed at low temperature (-20°C) or high temperature (45°C) for 0, 1, 2, 3, 4, 5, 8, 10, 12, 15, 17 and 19 days prior to use. At each timepoint, all test components were equilibrated to room temperature before initiating the test. Five replicates of the Negative and Positive Control swabs were tested at each timepoint. All tests produced expected results till day 12 for both temperature conditions. However, false results were observed at subsequent timepoints after storage at -20°C or 45°C. The results demonstrated that Nano-Check RSV Tests are stable for up to 12 days when stored at low temperatures (-20°C) or high temperatures (45°C).

  Labeling for Nano-Check RSV Test clearly states that tests should be stored at 2°C-30°C in the original sealed pouch and should not be frozen.

<u>Operator Errors in Performing the Test</u>

- *Effect of Sample Extraction Intensity – Depth of Swab Insertion:*

The Nano-Check RSV Test labelling instructs the user to insert the collection swab into the Reagent tube until the swab head touches the bottom of the tube for sample extraction. This study evaluated the following deviations to the test procedure:

1) swab head touching the Reagent tube bottom (control),
2) swab head inserted into the extraction buffer without touching the Reagent tube bottom, and
3) swab head not inserted into the extraction buffer.

Expected positive results were obtained both when the swab touched the tube bottom and when the swab head touched the extraction buffer without touching the tube bottom. However, when the swab did not touch the extraction buffer, it resulted in false negative results. All negative samples produced expected results for all testing conditions. The risk of the user not inserting the swab into the extraction buffer is mitigated through clear instructions and illustrations in the test procedure.

- *Effect of Inadequate Stirring of Swab in Extraction Buffer:*

The Nano-Check RSV Test procedure instructs the user to stir the sample swab at least 10 times in the extraction buffer in the Reagent tube. This study evaluated the risk of erroneous results when the swab is stirred:

1) 0 times
2) 5 times
3) 10 times (control)
4) 20 times

All samples yielded expected results, indicating that under or over stirring of the sample swab in the extraction buffer in the Reagent tube does not affect the test outcome.

- *Effect of Under-Squeezing the Swab Head:*

The Nano-Check RSV Test procedure instructs the user to squeeze the swab against the sides of the Reagent tube while removing it, to release the maximum amount of liquid from the swab. This study evaluated the risk of erroneous results when the swabs are removed without squeezing against the sides of the Reagent tube. All samples tested yielded expected results, indicating that forgetting to squeeze the sample swab head against the side of the Reagent tube when removing from the extraction buffer does not affect the test outcome.

- *Extraction Buffer Volume Variability:*

The Nano-Check RSV Test is provided with Reagent tubes containing 350 µL of extraction buffer. In this study, test samples were extracted in different volumes of the extraction buffer: 25% (87.5 µL), 50% (175 µL), 75% (263 µL), 100% (350 µL) and 125% (438 µL). The results showed that test results are not affected with a minimum volume of extraction buffer volume of 175 µL (50%). Expected results were also obtained when the buffer volume was at 438 µL (125%). However, extraction buffer

volume of 87.5 µL (25%) was insufficient volume for sample to flow across the membrane which requires two drops of extracted sample and resulted in invalid results. No erroneous results were observed. The study showed that even if 50% of the extraction buffer is inadvertently spilled, the test will generate accurate results.

- *Repeated Installing and Removing of Dropper Tip:*

  The Nano-Check RSV Test involves firmly pushing the provided Dropper tip to close the Reagent tube before applying the extracted sample onto the test device. Repeated installation and removal of the Dropper tip may cause the loss of contact between the Dropper tip and the Reagent tube, potentially causing a leakage. This study investigated this failure scenario by assessing the impact of varying Dropper tip installation on the Reagent tube up to 5 times. No buffer leakage was observed when applying two (2) drops of the extracted Negative and Weakly Positive samples after repeated Dropper tip installation. All samples yielded expected results up to five times of repeated installation and removal of the Dropper tip.

- *Errors in Sample Application – Effect of Sample Application Angle:*

  During the test procedure, the extracted sample is applied onto the test device through the provided Dropper tip. This study evaluated droplet size variation due to different holding angles of the Reagent tube over the sample well and its effect on the test results. Two drops of each sample were applied by holding the Reagent tube (a) vertically (as instructed in the test procedure), (b) at a 45° angle, and (c) horizontally. All samples yielded expected results when applied vertically and at a 45° angle. However, when the Reagent tube was held in the horizontal position, there was no sufficient volume in the tube to form proper droplets and, therefore, the test was not initiated. No erroneous results were generated.

  The risk of user not applying the sample properly to the test device is mitigated through the clear instructions and illustrations on how to hold the Reagent tube (vertically) in order to apply two drops of the sample into the sample well.

- *Errors in Sample Application – Sample Drop Volume Tolerance:*

  The Nano-Check RSV Test labeling instructs the user to squeeze the Reagent tube and dispense two drops of the sample into the sample well of the test device. This study evaluated the performance of the assay by varying the number of extracted sample drops applied to the test device's sample well. Ten replicates of each test sample were applied, using 1, 2, 3 and 4 drops. The results showed that insufficient sample volume (one drop) produced invalid results for both Weakly Positive (7/10) and Negative samples (8/10) and one false negative result (1/10) for Weakly Positive sample. Expected positive and negative results were obtained with both two and three droplets. Application of four drops led to flooding resulting in false negative results (3/10).

  The results showed that adding two drops of the sample is critical to the test performance. The risk of user not applying the sample properly to the test device is mitigated through the clear instructions and figures in the device labelling along with a precautionary note

that too few drops can result in invalid results and too many drops could produce incorrect results.

- *Extracted Sample Stability:*

  The test procedure consists of sequential steps where the sample extraction is followed by adding two drops of the sample mixture to the sample well of the test device. This study assessed the stability of the extracted sample in the extraction buffer, should the addition of the sample to the sample well be delayed. The samples were tested under two conditions: 1) with the sample swab left in the extraction buffer, and 2) after removing the swab post-extraction. The test samples were left at ambient conditions for 0 minute (control), 30 minutes and 60 minutes before being applied onto the Nano-Check RSV Test device. All samples yielded expected results across all the conditions tested, indicating that a delay in testing, after extraction in the buffer of up to one hour does not affect the test outcome. Nano-Check RSV Test labeling instructs the user that specimens in extraction buffer can be processed up to thirty minutes after collection when kept at room temperature.

- *In-Use (Open Pouch) Stability of Test Device:*

  Nano-Check RSV Test devices are supplied in aluminum pouches with desiccants. The stability of the test devices after opening the sealed pouch was assessed in this study. Upon opening, the test devices were exposed to ambient conditions for various durations: 0, 0.5, 1, 2, 3 and 4 hours. At each time point, 15 replicates of Weakly Positive samples and five replicates of Negative samples were tested. All samples yielded expected results across all the conditions tested in this study indicating that the waiting time up to 4 hours between opening the test device pouch and conducting the test does not affect the test outcome. The labeling of the Nano-Check RSV Test instructs the user that once opened, the test device should be used within 90 minutes.

- *Physical Impact Resistance of the Test – Shaking and Dropping of Test Device:*

  The study examined the effect of physical impact, introduced either by horizontal shaking of the test devices on the bench top or vertical dropping of the test devices from bench top to the floor during testing, at two different timepoints during the workflow – (a) immediately after addition of sample from the Reagent tube to sample well, or (b) five minutes after addition of sample to the test device. Ten replicates of each sample (Negative samples and Weakly Positive) were tested for each condition according to the test procedure. All devices tested yielded expected results for test devices that were shaken horizontally either immediately or after five minutes of sample addition to the sample well. For the test devices which were vertically dropped immediately after sample addition to the sample well, invalid results were reported for Weakly Positive (2/10) and Negative samples (1/10). However, all devices tested yielded expected results with the Negative sample and the Weakly Positive sample for the test devices that were dropped vertically after five minutes of sample addition to the sample well. No erroneous results were observed. These errors are mitigated by clear labeling which instructs the user to conduct all testing on a level surface.

- *Incorrect Timing of Reading Results:*

  The test procedure specifies that test results can be read visually between 15 and 20 minutes after the sample is added to the sample well on the test device. This study evaluated reading the results visually after 3, 7, 10, 15, 30, 45 and 60 minutes after addition of sample to the sample well. Ten replicates of Negative and Weakly Positive samples were tested at each timepoint in this study. All Weakly Positive samples produced expected positive results at or after 10 minutes from sample application. Weakly Positive samples read at 3 and 7 minutes after sample application resulted in false negative results (10/10 at 3 minutes and 3/10 at 7 minutes). No false positives were observed with Negative samples until 60 minutes after sample application. To minimize the potential occurrence of false negative or false positive results, the test procedure instructs the user to read the test results at 15 minutes after sample application, and no later than 20 minutes after sample application.

Environmental conditions

- *Environmental Tolerance – Temperature:*

  The labeling specifies optimum conditions for performing the test to be room temperature (15°C to 30°C). The purpose of this study was to evaluate the effect of high (40°C) and low (10°C) temperature on the test performance of the Nano-Check RSV Test. Thermal control chambers were used to simulate the test conditions. Ten replicates each of Weakly Positive and Negative samples were used as test inputs for the condition described above. All pouched test devices/Reagent tubes/Negative and Weakly Positive swabs were placed in the thermal chamber and allowed to equilibrate with the chamber temperature prior to testing. All samples generated expected results at both 10°C and 40°C, demonstrating that the risks of erroneous results due to extremes of temperature outside the specified conditions are minimal.

- *Environmental Tolerance – Humidity:*

  The purpose of this study was to evaluate the effect of humidity [35% (Ambient), <20% (Low), >90% (High)] on the test performance of the Nano-Check RSV Test. Humidity controlled areas were used to simulate the test conditions. All pouched test devices/Reagent tubes/Negative and Weakly Positive swabs were placed in either the ambient conditions or inside the humidity-controlled areas and allowed to equilibrate prior to testing. Ten replicates of Weakly Positive and Negative samples were tested at the conditions described above. All samples generated expected results demonstrating that the risks of erroneous results due to extremes of humidity are minimal.

- *Incorrect Placement of Device: Test Run on Uneven Surfaces and Severe Angles:*

  The purpose of this study was to evaluate the effect of non-leveled benchtop or work surface on the test performance of the Nano-Check RSV Test. Five replicates of each sample (Negative and Weakly Positive) per condition were tested in the study according to the test procedure. Testing was carried out on surfaces inclined at 0° (control), 10°, 20°, or 30°, with the test device oriented either upward or downward. It was observed

that the applied sample flooded into the observation window when the test device was tilted 30° downward. Additionally, when the device was tilted 30° upward, it was observed that the sample could not be absorbed completely. However, each of the four angles, both with the test device upward and downward, produced expected results for all Negative and Weakly Positive samples tested. The risks of any potential erroneous results are mitigated by clear directions in the labeling, which directs users to conduct all testing on a level surface and at ambient conditions.

- *Effect of Vibrations:*

  The purpose of this study was to evaluate whether vibration of the test device after sample application will impact the test performance of the Nano-Check RSV Test. Five replicates of each sample (Negative and Weakly Positive) were tested in the study by placing the test device after sample application on microplate shakers at different speeds: 0, 100, 300 and 500 rpm for the duration of the test (15 minutes). All samples generated expected results demonstrating that the risks of erroneous results due to vibrations during testing are minimal.

- *Effect of Light – Bright or Dark Conditions:*

  The purpose of this study was to evaluate the effect of varying levels of light on the test performance of the Nano-Check RSV Test. The study was conducted in a blinded manner by three operators, each testing five replicates of each sample (Negative and Weakly Positive) per illumination level. Testing was carried out under four different illumination conditions produced by using either an incandescent lamp or natural sunlight, to simulate: 1) 10-15 Lux (after dusk), 2) 500-1000 Lux (shaded sunlight), 3) 2000-2500 Lux (under an incandescent lamp) and 4) >50,000 Lux (natural sunlight). False negative results (4/15) were observed with Weakly Positive samples when light intensity was 10-15 Lux (after dusk). All samples returned expected results when the light intensity was at 500-1000 Lux or higher. The risk of potential erroneous results due to poor lighting conditions is mitigated by clear directions in the labeling: Ensure that testing and result interpretation is conducted in a well-lit space with sufficient lighting.

Conclusion from Flex Studies

The flex studies carried out in support of this CLIA waiver submission have effectively and comprehensively demonstrated the robustness of the system to generate correct results even when operated under conditions of stress. The combination of the device design and the built-in fail-safe features, along with the clear test instructions which include relevant cautions, render the risks of erroneous results to be minimal. As all identified sources of user errors have been addressed either by fail-safe features, failure alert mechanisms or labeling mitigations, Nano-Check RSV Test was shown to have an insignificant level of risk of generating erroneous results when used according to the test procedure instructions.

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

Clinical Performance

- *Study Design*

i. Study Sites and Duration:
Clinical performance characteristics of Nano-Check RSV Test were evaluated in a multi-site prospective study between November 2023 and March 2024, during the respiratory season within the United States. Six (6) geographically diverse sites, including urgent care clinic, physicians' offices and adult care center participated in the clinical study. All the sites qualified as representative of CLIA waived intended use sites for this device.

ii. Operators:
A total of nine (9) operators representative of intended CLIA waived users participitated in the study across the six clinical testing sites. The participants consisted of medical staff personnel providing patient care and included medical assistants, nurses, office manager and a physician. The test operators who participated in the study were untrained in the use of the Nano-Check RSV Test and had no hands-on experience with conducting diagnostic testing in a clinical laboratory. Information on the operators' current job title, education, laboratory experience and the number of years of relevant work experience was provided. The education of the operators ranged from high school graduates to graduate degrees. Operators were provided only with the instructions for use and the Quick Reference Instructions.

iii. Subjects:
Specimens for the prospective clinical study were collected under informed consent or, if the subject was <7 years of age, with parental permission and assent of the participant. Demographic and clinical data were collected from subjects by interview and medical record review. The subjects were enrolled according to the Inclusion or Exclusion criteria in the study protocol and included pediatric subjects from 6 months to 6 years of age and adult subjects 60 years and older.

iv. Samples:
Two anterior nasal (AN) swabs were collected sequentially from each subject. The first swab (for comparator testing) was collected by the study operator from both sides of the nose and placed into transport media for comparator testing. These swab samples were shipped to a reference testing laboratory, where they were tested on the comparator method following the product's IFU. The second swab was collected by the study operator from both sides of the nose and tested immediately with the Nano-Check RSV Test at the site.

A total of 886 patients were enrolled in the clinical study of which 68 were excluded due to protocol deviations, leaving 818 specimens to be included in the calculations of estimates of assay performance. Specimens were collected from pediatric patients between 6 months to 6 years of age and adult patients 60 years or older. Of those, 29% (237/818) were from subjects 6 months to 2 years old, 36.9% (302/818) were from patients 2 to 6 years of age and 34.1% (279/818) were from patients 60 years or older. There were 52.4% (429/818) females and 47.6% (389/818) males.

v. Comparator Method:

The performance of the Nano-Check RSV Test with AN swabs was estimated based on the comparison with results obtained with an FDA cleared molecular test for RSV and is presented as positive percent agreement (PPA) and negative percent agreement (NPA) shown below.

- *Clinical Study Results*

The clinical performance of the Nano-Check RSV Test, when used by untrained operators, testing AN swabs from patients with symptoms of respiratory tract infection, is shown in table below. No invalid results were obtained during the clinical study.

Clinical Performance of Nano-Check RSV Test with AN Swabs

Nano-Check RSV Test	Comparator RT-PCR		Total
	Positive	Negative	
Positive	93	3	96
Negative	18	704	722
Total	111	707	818
Positive Percent Agreement (PPA) = 83.8% (95% CI: 75.8% - 89.5)			
Negative Percent Agreement (NPA) = 99.6% (95% CI: 98.8% - 99.9%)			

Device Performance with Analyte Concentrations Near the Cutoff

The performance of the Nano-Check RSV Test with samples at analyte concentrations near the assay cutoff was evaluated in a study conducted at three external sites representative of CLIA waived sites, with a total of seven untrained operators and at one internal site with three trained operators. The test samples were contrived in negative clinical matrix (NCM) at four concentration levels: true negative (composed of NCM only), high negative (0.1x LoD, or 1.6×10^2 $TCID_{50}$/mL), low positive (1x LoD, or 1.6×10^3 $TCID_{50}$/mL), and positive (3x LoD, or 4.8×10^3 $TCID_{50}$/mL). Blinded operators tested a randomized coded panel of contrived samples, with three replicates per level per operator being tested across five days. Testing was performed according to the test instructions in the QRI.

No invalid test results were obtained during the study. The percent agreement with the expected results for each panel member, stratified by site, is summarized in the table below. The table below includes the rate of RSV detection for weakly reactive samples when the test was used by untrained intended users. Also provided is the rate of RSV detection for weakly reactive samples in the hands of trained laboratorians at one clinical laboratory site.

Summary of Results Testing Samples with Analyte Concentrations Near the Cutoff with the Nano-Check RSV Test

Site	Operator	Expected Result: Negative		Expected Result: Positive	
		True Negative (NCM only)	High Negative (0.1x LoD)	Low Positive (1x LoD)*	Positive (3x LoD)
Site 1 (External)	n=2 Untrained	30/30	30/30	30/30	30/30
Site 2 (External)	n=3 Untrained	45/45	45/45	45/45	45/45

Site 3 (External)	n=2 Untrained	30/30	30/30	30/30	30/30
Site 4 (Internal)	n=3 Trained	45/45	45/45	45/45	45/45
Total		150/150	150/150	150/150	150/150
Agreement with Expected Results		100%	100%	100%	100%
95% CI		97.5-100%	97.5-100%	97.5-100%	97.5-100%

*While the Low Positive sample used in the study, at an LoD concentration 1.6×10^3 $TCID_{50}$/mL, generated 100% positivity, the subsequent 1:2 dilution of this sample to 8.0×10^2 $TCID_{50}$/mL demonstrated 30% positivity.

The study results demonstrated that users untrained in the test procedure of the Nano-Check RSV Test were able to perform the test correctly and the test provided the expected results for samples with organism concentration near the assay cutoff. Further, the study demonstrated that untrained users can perform the test with the same accuracy as the trained users.

Operator Questionnaire

Following completion of the study, operators at each site were asked to complete a questionnaire to help assess whether participants understood how to use the Nano-Check RSV Test correctly. The questionnaire consisted of a series of questions pertaining to the ease of use of the test with answers rated on a scale from one to five where five indicated the greatest ease of use and one indicated the least ease of use. Participants graded the overall ease of use at a rating ranging from 4 to 5. They found the test to be easy to use and the instructions easy to understand. Based on the operators' feedback, the results were easy to interpret.

D Labeling for Waived Devices

The labeling consists of:

1. Product Insert
2. Quick Reference Instructions (QRI)

The following elements are appropriately present:

- The Quick Reference Instructions are written in simple language and, where appropriate, contain graphic representation of system components and procedure steps.
- The labeling identifies the test for prescription use only.
- The labeling contains a statement that a Certificate of Waiver is required to perform the test in a waived setting.
- The labeling identifies the sample type that may be used in Waived Settings.
- The labeling contains a statement that laboratories with a Certificate of Waiver must follow the manufacturer's instructions for performing the test.
- The Quick Reference Instructions provides instructions for conducting quality control procedures.
- The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

XI. Benefit-Risk Considerations

Based on the benefit-risk assessment, the risk of harm to a patient using the Nano-Check RSV Test in CLIA-waived setting is anticipated to be low. The performance of the test is within the same range of the performance as the other antigen tests that are currently CLIA-waived. Also, the use of anterior nasal swabs as the specimen type for the Nano-Check RSV test is likely to reduce patient inconvenience and discomfort with testing in the doctor's office and help ensure optimal specimen collection. Therefore, the Nano-Check RSV test has a favorable benefit-risk profile, making its use in a CLIA-waived setting medically acceptable.

XII. Conclusion

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