# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY ONLY

## I Background Information:

### A 510(k) Number

K221664

### B Applicant

Aardvark Medical, Inc.

### C Proprietary and Established Names

CLEARinse CTS Specimen Collection and Transport System

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| QBD | Class II | 21 CFR 866.2950 - Microbial Nucleic Acid Storage And Stabilization Device | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:
To obtain a substantial equivalence determination for the CLEARinse CTS Specimen Collection and Transport System for the collection and transport of nasal wash aspirate speciments that may contain inflenza A or influenza B viruses.

### B Measurand:
Nucleic acids and antigens from influenza A and influenza B viruses.

### C Type of Test:
Microbial nucleic acid and antigen collection, transport, and storage device.

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

### B Indication(s) for Use:

CLEARinse CTS is intended to collect and transport clinical nasal wash aspirate specimens that may contain influenza A or influenza B virus, by health care professionals, from the collection site to a laboratory or testing site. CLEARinse CTS specimens are suitable for use with legally marketed lateral flow immunoassays and molecular assays. CLEARinse CTS is for professional in-vitro diagnostic use.

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

### D Special Instrument Requirements:

## IV Device/System Characteristics:

### A Device Description:

CLEARinse CTS Specimen Collection and Transport System consists of a CLEARinse Pro Handle and CLEARinse CTS Wash Head and is intended to collect and transport nasal wash aspirate (NWA) specimens that may contain influenza A or influenza B virus by health care professionals (See Figure 1 below). The CLEARinse CTS Wash Head is completely disposable to allow for the safe collection and transportation of the preserved specimen and safe disposal after use.

To use the CLEARinse CTS, a 3-mL ampule of 0.9% sterile saline is placed into the irrigation chamber of the wash head. The wash head is then assembled onto the CLEARinse handle by the health care provider (HCP). The specimen chamber of the CLEARinse CTS wash head will then contain the NWA sample that may be used for future testing. The wash head is then removed from the handle. A specimen collected in the wash head may be used for testing if immediately, or the wash head can be placed into the CLEARinse CTS Transport Container and sent to a laboratory for testing. CLEARinse CTS Wash Head specimens can only be processed using validated or verified clinical operating procedures using legally marketed lateral flow immunoassays or molecular assays. CLEARinse CTS is for professional in-vitro diagnostic use.

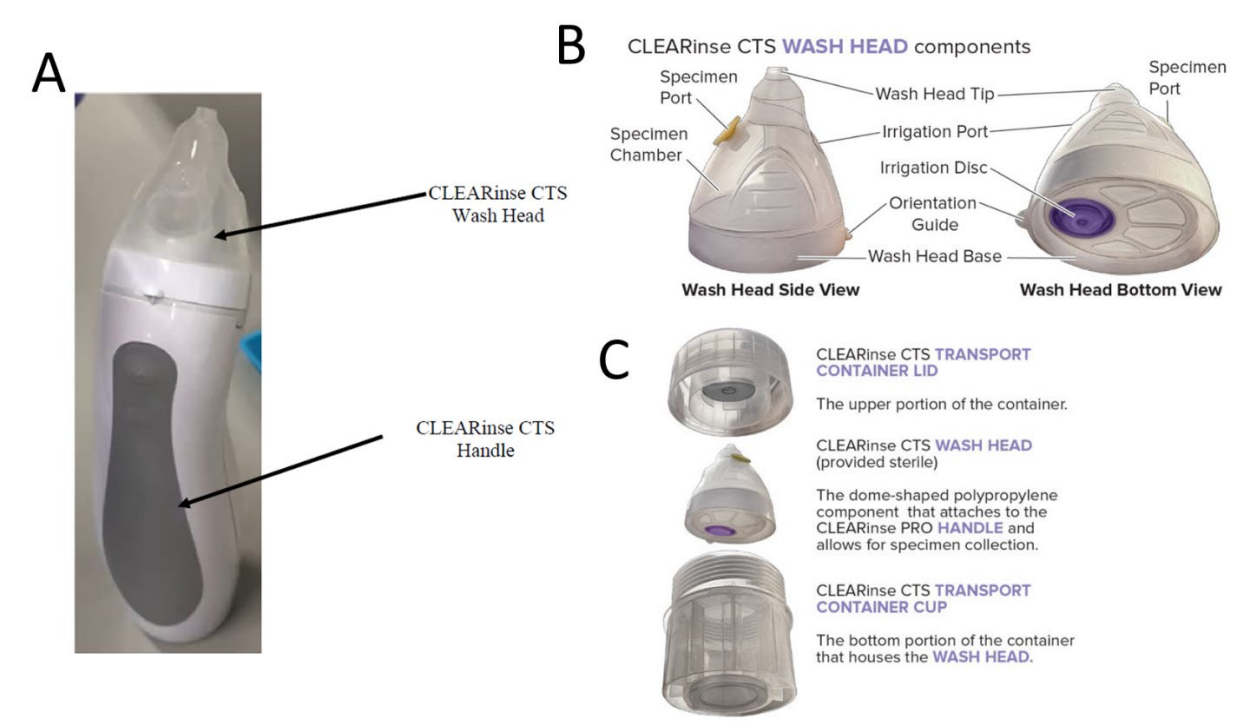


Figure 1. (A) FDA-cleared (K082762) CLEARinse Pro System, (B) CLEARinse CTS Wash Head, and (C) CLEARinse CTS components.

**B Principle of Operation:**

CLEARinse CTS enables the collection and transport of NWA specimens from a patient presenting with influenza-like illness. The sterile, single-use wash head is attached to the pneumatic-pump handle before the contents of a saline ampoule are squeezed into the irrigation port of the wash head. The tip of the wash head is then inserted into the patient's nostril and sterile saline is introduced by repeatedly pressing the irrigate button. The irrigated saline and nasal secretions are then aspirated back through the opposite nostril back into the CLEARinse CTS wash head. This specimen can be drawn from the wash head for immediate testing, or the wash head may be placed into the transport container, which seals the wash head for transport to the testing site.

## V Substantial Equivalence Information:

**A Predicate Device Name(s):**
PrimeStore MTM

**B Predicate 510(k) Number(s):**
DEN170029

**C Comparison with Predicate(s):**

| **Device & Predicate Device(s):** | Subject: K221664 | Predicate: DEN170029 |
|---|---|---|
| Device Trade Name | CLEARinse CTS: Specimen Collection | PrimeStore MTM |

| | | |
|---|---|---|
| | and Transport System | |
| **General Device Characteristic Similarities** | | |
| Intended Use/Indications For Use | CLEARinse CTS is intended to collect and transport clinical nasal wash aspirate specimens that may contain influenza A or influenza B virus, by health care professionals, from the collection site to a laboratory or testing site. CLEARinse CTS specimens are suitable for use with legally marketed lateral flow immunoassays and molecular assays. CLEARinse CTS is for professional in-vitro diagnostic use. | PrimeStore MTM is intended for the stabilization, transportation and inactivation of infectious unprocessed nasal washes suspected of containing Influenza A virus RNA. PrimeStore MTM is also intended for the stabilization, transportation and inactivation of infectious unprocessed sputum samples suspected of containing *Mycobacterium tuberculosis* DNA from human samples. |
| Material | Polypropylene | Same |
| **General Device Characteristic Differences** | | |
| Specimen Type | Nasal Wash Aspirate suspected of containing Influenza A or B viruses | Nasal wash suspected of containing Influenza A virus. Sputum samples suspected of containing MTB. |
| Transport Media formulation | 0.9% saline from nasal wash | Nucleic Acid Stabilization solution |
| Device Material Supplied | Wash Head and Transport Container | Molecular Transport Medium provided in cryogenic tube |
| Sterility | Sterile | Not sterile |
| Inactivation | No inactivation of viruses or bacteria | Inactivation of influenza A and MTB by Guanidine thiocyanate |
| Specimen Collection | Collection using the CLEARinse Pro Handle and Instructions for Use | Collection using standard clinical procedures |

## VI Standards/Guidance Documents Referenced:

Special controls that are applicable to regulation 21 CFR 866.2950

Sterilization standards: ANSI/AAMI/ISO 11737-1:2018 and ANSI/AAMI/ISO 11737-2:2019

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

   N/A

2. Linearity:

   N/A

3. Analytical Specificity/Interference:

   N/A

4. Assay Reportable Range:

   N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   **Shelf Life:** The shelf life for the CLEARinse CTS Wash Head was evaluated in a real-time stability study. The predefined acceptance criteria between time point zero and eight (8) months. Tests that were passed included 1) visual packaging integrity inspection (visual verification the packaging integrity, sterile barrier, and the system was usable with no obvious conditions that would prevent the use of the system as intended), 2) air flow test (verification the system aspiration airflow was within the range of 8.0 to 10.0 L/min), 3) aspiration pressure test (verification the system aspiration pressure was in the range of 80 to 120 mmHg), and 4) irrigation actuation volume test (verification the injection volume was in the range is 0.25ml to 0.50ml per actuation of the irrigation plunger).

   **Sterilization:** The CLEARinse CTS Wash Head is labeled a sterile device. As part of sterility testing, a bioburden study was first conducted with microbial identification determined for the three most predominant isolates (*Bacillus simplex, B. cerus*, and *B. licheniformis*) following the standard ISO 11737-1 Third edition.

   Ten CTS Wash Heads units were chosen from each of the three lots used for sterilization testing. Each lot was sterilized with irradiation (East A) (following standard ISO 11137-2: 2013) with a validation method used for the sterilization cycle (of 25 kGy dose). Irradiated

devices were cultured for 14 days with none of the samples exhibiting growth. The data supported a Sterility Assurance Level (SAL) of $10^{-6}$.

6. Detection Limit

A Limit of Detection (LoD) study was conducted to determine the lowest concentration of Influenza A and Influenza B that contains measurable nucleic acids or measurable antigens. Recovery of target analyte from the transport media, with a greater than 95% accuracy, was assessed by spiking pooled negative clinical nasal wash matrix (NWA and 0.9% saline solution) with various concentrations of Influenza nucleic acid or antigen. The contrived samples were then placed into and removed from the Wash Head. The recovered samples are then placed into the workflow for the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV and BioSign Flu A+B assays. The results are compared to established LoD for the reference assays, found in their respective Package Inserts (PI).

**A. PCR LoD Test Results:**
Preliminary LoD testing was initially performed by spiking multiple concentrations of three different strains of influenza into NWA. The three viral concentrations used were 3X, 1X, and 0.5X of the established LoDs of similar influenza strains (Table 1) in the PI for the reference assay. The assay used was the EUA authorized Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge using the GeneXpert Xpress System. Positive and negative results were determined as explained in the PI for the device.

**Table 1.** Proposed test levels for Cepheid PCR testing for preliminary LoD study

| Virus Type | Strain tested with CTS device | Reported LoD of Similar Strain* |
|---|---|---|
| Influenza A, H1N1 | A/Netherlands/606/2009 | 4.0 x $10^{-3}$ $TCID_{50}$/mL for A/California/7/2009(H1N1) |
| Influenza A, H3N2 | A/Indiana/10/2011 | 8.7 x $10^{-2}$ $TCID_{50}$/mL for A/Victoria/361/2011(H3N2) |
| Influenza B | B/Florida/07/2004 | 4.0 x $10^{-2}$ $TCID_{50}$/mL for B/Massachusetts/2/2012 |

*Note: strains used to determine analytical sensitivity (LoDs) for validation of the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV Cartridge

For the Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV PCR test, LoD range-finding results indicated that the Influenza A (FluA) samples contrived by the sponsor performed similarly to those used by Cepheid to establish the reported LoDs. For both FluA viruses, all three replicates were positive at 1X and 3X the reported LoD (Table 2). At 0.5X the reported LoD, each virus was negative for one or more replicates, indicating that the 1X level was truly near the LoD using the viral stocks listed in table 1. For the influenza B (FluB), testing at 10-fold lower levels (0.05X – 0.3X) resulted in similar qualitative results: all three replicates positive at 0.1X and 0.3X, and only two of three replicates positive at 0.05X (Table 2).

**Table 2.** Preliminary PCR LoD Estimation Results with individual LoDs highlighted in grey.

| Flu Type | Test Level | | Qualitative Results | | Mean Ct* |
|---|---|---|---|---|---|
| | Description | $TCID_{50}$/mL | # Positive | % Positive | |
| FluA H1N1 | 3X | 1.2E-02 | 3 of 3 | 100% | 34.9 |
| | 1X | 4.0E-03 | 3 of 3 | 100% | 36.8 |
| | 0.5X | 2.0E-03 | 2 of 3 | 67% | 37.4 |
| FluA H3N2 | 3X | 2.6E-01 | 3 of 3 | 100% | 35.6 |
| | 1X | 8.7E-02 | 3 of 3** | 100% | 36.9 |
| | 0.5X | 4.3E-02 | 0 of 3 | 0% | N/A |
| FluB | 0.3X | 1.2E-02 | 3 of 3 | 100% | 36.0 |
| | 0.1X | 4.0E-03 | 3 of 3 | 100% | 38.8 |
| | 0.05X | 2.0E-03 | 2 of 3 | 67% | 38.1 |

*Note: Mean Ct for FluA viruses are calculated based on the FluA1 analyte, which produced a consistent Ct values.
** **One replicate was positive on FluA1 and was negative on FluA2 and was considered below the LoD.

Confirmatory LoD testing was conducted with 20 replicates using contrived samples. The samples for the confirmatory were contrived using the sample procedure that was used for the preliminary study. The Ct values for the 20 replicates of the confirmatory tests for each of the three influenza strains are shown in tables 3-5.

**Table 3.** PCR LoD Confirmation Results for Influenza A H1N1

| Concentration (1X LoD) | Replicate | FluA 1 Result | FluA 1 Ct | FluA 2 Ct |
|---|---|---|---|---|
| 4.00E-03 | 1 | Positive | 35.8 | 36.7 |
| 4.00E-03 | 2 | Positive | 35.2 | 36.4 |
| 4.00E-03 | 3 | Positive | 35.3 | 37 |
| 4.00E-03 | 4 | Positive | 38 | 41.1 |
| 4.00E-03 | 5 | Positive | 35.1 | 36.5 |
| 4.00E-03 | 6 | Positive | 36 | 37.8 |
| 4.00E-03 | 7 | Positive | 35.7 | 38.2 |
| 4.00E-03 | 8 | Positive | 35.9 | 40 |
| 4.00E-03 | 9 | Positive | 36.5 | 37.8 |
| 4.00E-03 | 10 | Positive | 35.6 | 37.2 |
| 4.00E-03 | 11 | Positive | 36.9 | 38.6 |
| 4.00E-03 | 12 | Positive | 35.4 | 36.8 |
| 4.00E-03 | 13 | Positive | 32.2 | 34.3 |
| 4.00E-03 | 14 | Positive | 35.2 | 36.1 |
| 4.00E-03 | 15 | Positive | 34.4 | 35.3 |
| 4.00E-03 | 16 | Positive | 36 | 38.6 |

| | | | | |
|---|---|---|---|---|
| 4.00E-03 | 17 | Positive | 34.9 | 36.7 |
| 4.00E-03 | 18 | Positive | 36.3 | 37.8 |
| 4.00E-03 | 19 | Positive | 35.3 | 37.2 |
| 4.00E-03 | 20 | Positive | 35.5 | 37.3 |

**Table 4.** PCR LoD Confirmation Results for Influenza A H3N2

| Concentration (1X LoD) | Replicate | FluA 1 Result | FluA 1 CT | FluA 2 CT |
|---|---|---|---|---|
| 2.60E-01 | 1 | Positive | 37.1 | ND |
| 2.60E-01 | 2 | Positive | 36.1 | 40 |
| 2.60E-01 | 3 | Positive | 37.7 | 39 |
| 2.60E-01 | 4 | Positive | 35.1 | 37 |
| 2.60E-01 | 5 | Positive | 35.4 | 43 |
| 2.60E-01 | 6 | Positive | 34.3 | 37 |
| 2.60E-01 | 7 | Positive | 35.3 | ND |
| 2.60E-01 | 8 | Positive | 35.5 | 38 |
| 2.60E-01 | 9 | Positive | 35.3 | 39 |
| 2.60E-01 | 10 | Positive | 35 | 37 |
| 2.60E-01 | 11 | Positive | 35.2 | 39 |
| 2.60E-01 | 12 | Positive | 35.8 | 38 |
| 2.60E-01 | 13 | NA* | NA* | NA* |
| 2.60E-01 | 14 | Positive | 35.2 | 38 |
| 2.60E-01 | 15 | Positive | 35.6 | 38 |
| 2.60E-01 | 16 | Positive | 36 | 39 |
| 2.60E-01 | 17 | Positive | 35.3 | 39 |
| 2.60E-01 | 18 | Positive | 35.6 | 39 |
| 2.60E-01 | 19 | Positive | 35.5 | 38 |
| 2.60E-01 | 20 | Positive | 34.9 | 37 |
| 2.60E-01 | 21 | Positive | 35.5 | 41 |

*Note: Error. Probe check failed with the output of "NO RESULT – REPEAT TEST." Replicate was repeated and positive results were obtained.

**Table 5.** PCR LoD Confirmation Results for Influenza B

| Concentration (1X LoD) | Replicate | FluB Result | FluB CT |
|---|---|---|---|
| 4.00E-03 | 1 | Positive | 36.1 |
| 4.00E-03 | 2 | Positive | 36.1 |
| 4.00E-03 | 3 | Positive | 36.1 |
| 4.00E-03 | 4 | Positive | 36.3 |
| 4.00E-03 | 5 | Positive | 36.5 |
| 4.00E-03 | 6 | Positive | 36.7 |
| 4.00E-03 | 7 | Positive | 36.3 |
| 4.00E-03 | 8 | Positive | 36.2 |
| 4.00E-03 | 9 | Positive | 36.9 |
| 4.00E-03 | 10 | Positive | 36.2 |
| 4.00E-03 | 11 | Positive | 35.8 |

| | | | |
|---|---|---|---|
| 4.00E-03 | 12 | Positive | 35.9 |
| 4.00E-03 | 13 | Positive | 35.7 |
| 4.00E-03 | 14 | NA* | NA* |
| 4.00E-03 | 15 | Positive | 36.3 |
| 4.00E-03 | 16 | Positive | 36.6 |
| 4.00E-03 | 17 | Positive | 39.2 |
| 4.00E-03 | 18 | Positive | 36.4 |
| 4.00E-03 | 19 | Positive | 35.9 |
| 4.00E-03 | 20 | Positive | 37.1 |
| 4.00E-03 | 21 | Positive | 36.4 |

*Note: Error. Probe check failed with the output of "NO RESULT – REPEAT TEST." Replicate was repeated and positive results were obtained.

In summary, the testing performed established that for PCR assays 4 $x10^{-3}$ $TCID_{50}$/mL is the LoD for both Influenza A(H1N1) and B, and that 2.6 $x10^{-1}$ $TCID_{50}$/mL is the LoD for Influenza A(H3N2).

**B. LFA LoD Test Results:**

An initial LoD range-finding study was conducted with the BioSign Flu A+B lateral flow assay (LFA). The preliminary results indicated that additional antigen concentrations needed to be tested beyond the initially planned levels of 0.5X, 1X, and 3X of the reported LoD. For influenza A H1N1, all replicates produced positive results at all test levels, so an additional lower level (0.125X) was tested. For influenza A H3N2 and influenza B, all levels initially tested produced negative results for all three replicates. Thus, higher levels were tested until a test level produced three of three positive results. A summary of levels tested and the results at each level are presented in table 6.

**Table 6.** LFA LoD Range-Finding Results

| Flu Type | Test Level | | Qualitative Results | |
|---|---|---|---|---|
| | Description | $TCID_{50}$/mL | # Positive | % Positive |
| FluA H1N1 | 0.5X | 5.25E+01 | 3 of 3 | 100% |
| | 0.25X | 2.63E+01 | 3 of 3 | 100% |
| | 0.125X | 1.32E+01 | 0 of 3 | 0% |
| FluA H3N2 | 27X* | 2.65E+03 | 3 of 3 | 100% |
| | 20X | 1.99E+03 | 0 of 3 | 0% |
| | 10X | 9.95E+02 | 0 of 3 | 0% |
| FluB | 20X | 3.98E+02 | 3 of 3 | 100% |
| | 10X | 1.99E+02 | 0 of 3 | 0% |
| | 3X | 5.97E+01 | 0 of 3 | 67% |

*Note: LoD is lower than for confirmatory studies below (Table 7) because of a miscalculation in preparation of H3N2 analyte for the range-finding study.

Confirmatory Lod testing was conducted with 20 replicates using contrived samples. The samples for the confirmatory testing were contrived using the sample procedure that was used for the preliminary study. For all three viral test strains the lowest concentration that produced at least 19 positives out of 20 samples (95%) was determined to be the LoD for each test strain (table 7).

**Table 7.** LFA LoD Confirmation Results

| Flu Type | Test Level | | Qualitative Results | |
|---|---|---|---|---|
| | Description | $TCID_{50}$/mL | # Positive | % Positive |
| FluA H1N1 | 0.25X | 2.63E+01 | 20 of 20 | 100% |
| FluA H3N2 | 40X* | 3.98E+03 | 20 of 20 | 100% |
| FluB | 20X | 3.98E+02 | 20 of 20 | 100% |

*Note: Confirmatory testing for FluA strain H3N2 was performed at a higher LoD than the range-finding LoD study.

In summary, the testing performed established that 4 x10-3 $TCID_{50}$/mL is the LoD for both Influenza A(H1N1) and B, and that 2.6 $x10^{-1}$ $TCID_{50}$/mL is the LoD for Influenza A(H3N2).

7. Specimen Stability

**Stability:**

**A. Viral nucleic acid stability**

Contrived samples containing Influenza strains at a concentration of 2.5X LoD were prepared in pooled NWA matrix. Sample stability was evaluated in a study in which each device contained 2 mL of virus inoculum in NWA. The spiked NWA was subsequently placed in a sealed CLEARinse CTS Transport Container and incubated at 4ºC and 27ºC for various timepoints. Testing of the contrived samples was conducted at time point zero to establish a baseline and again at 4 hours, 6 hours, 24 hours, and 48 hours. Aliquots of each contrived sample was tested for Influenza using Cepheid Xpert Xpress SARS-CoV-2/Flu/RSV Cartridges. Each PCR assay was performed in triplicate for each time point and for each storage condition. Samples were not batched, and all testing was completed immediately upon removal of sample from the Wash Head following the instructions in the respective package inserts. The acceptance criteria for the stability study included a deviation of no more than +/- 3 Ct for each target at given time point from T = 0

Results of stability testing for each of the three Influenza strains are shown below in table 8 below.

**Table 8.** Specimen Stability Study - PCR amplification from CLEARinse CTS Containers

| Virus and LoD | Storage Temp | Average Ct value | | | | |
|---|---|---|---|---|---|---|
| | | 0-hr | 4-hr | 6-hr | 24-hr | 48-hr |
| FluA H1N1 | 4ºC | NT | 35.6 | 36 | 36 | 36.7 |
| 2.5X LoD | 27ºC | 34.6 | 35.8 | 34.8 | 34.9 | 36.9 |
| FluA H3N2 | 4ºC | NT | 35.1 | 35.6 | 35.4 | 36 |
| 2.5X LoD | 27ºC | 35.4 | 35.6 | 35.8 | 36.1 | 36.4 |
| FluB | 4ºC | NT | 36.7 | 36.1 | 37.8 | 37.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5X LoD | 27ºC | 36.3 | 36.4 | 37.6 | 37.2 | 38.5 |

In summary, these data support the claim that samples for viral nucleic acid testing are stable when stored for 48 hours at room temperature and when refrigerated temperature.

**B. Viral Antigen Stability**

Contrived samples containing Influenza strains at a concentration of 2.5X LoD were prepared in pooled NWA matrix. Sample stability was evaluated in a study in which each device contained 2 mL of virus inoculum in NWA. The spiked NWA was placed in a sealed CLEARinse CTS Transport Container and incubated at 4ºC and 27ºC for various timepoints. Testing of the contrived samples were conducted at time point zero to establish a baseline and again at 4 hours, 6 hours, 24 hours, and 48 hours. Aliquots of each contrived sample was tested for influenza using Princeton BioMeditech Corporation BioSign Flu A + B test kits. Each LFA assay was performed in triplicate for each time point and for each storage condition. Samples were not batched, and all testing was completed immediately upon removal of sample from the Wash Head following the instructions in the respective package inserts.

Results of stability testing for each of the three Influenza strains are shown below in table 9 below.

**Table 9.** LFA Results from CTS Devices at 2.5X LoD

| Virus | Storage Temp | Number of positive samples out of replicates with valid results | | | | |
|---|---|---|---|---|---|---|
| | | 0-hr | 4-hr | 6-hr | 24-hr | 48-hr |
| FluA H1N1 | 4ºC | NT | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 |
| | 27ºC | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 | |
| FluA H3N2 | 4ºC | NT | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 |
| | 27ºC | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 | |
| FluB | 4ºC | NT | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 |
| | 27ºC | 3 of 3 | 3 of 3 | 3 of 3 | 3 of 3 | |

In summary, these data support the claim that samples that will be used for antigen testing are stable when stored for 24 hours at room temperature or 48 hours refrigerated.

8. Assay Cut-Off:

N/A

**B Comparison Studies:**

1. Method Comparison with Predicate Device:

N/A

2. Matrix Comparison:

N/A

**C Clinical Studies:**

1. Clinical Sensitivity:

   N/A

2. Clinical Specificity:

   N/A

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   N/A

**D Clinical Cut-Off:**

N/A

**E Expected Values/Reference Range:**

N/A

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.