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

## I Background Information:

### A 510(k) Number

K202641

### B Applicant

Zymo Research

### C Proprietary and Established Names

DNA/RNA Shield Collection Tube

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| QBD | Class II | 21 CFR 866.2950 - | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

To make a substantial equivalence determination for the Zymo Research DNA/RNA/ Shield Collection Tube for the collection, transport and storage of viral specimens to the laboratory for downstream testing.

### B Measurand:

Storage and stability of nucleic acids from SARS-CoV-2.

### C Type of Test:

Microbial nucleic acid storage and stabilization device

## III Intended Use/Indications for Use:

### A Intended Use(s):
See Indications for Use below.

### B Indication(s) for Use:
The DNA/RNA Shield™ collection tube is intended for the stabilization and inactivation of upper and lower respiratory human specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at ambient temperatures (20-25°C). Specimens collected and stored in a DNA/RNA Shield™ collection tube are suitable for use with legally marketed molecular diagnostic devices.

### C Special Conditions for Use Statement(s):
[Choose Rx or OTC]

Rx

### D Special Instrument Requirements:

None

## IV Device/System Characteristics:

### A Device Description:

The DNA/RNA Shield collection tube and reagent consists of a tube pre-filled with DNA/RNA Shield transport media. DNA/RNA Shield is a transport media that ensures stability of SARS-CoV-2 RNA during sample transport/storage at ambient temperatures and is intended to inactivate SARS-CoV-2, effectively lyses cells from collected upper and lower respiratory sputum specimens. The Zymo DNA/RNA Shield consists of a tube with a screw top containing 2 mL of media for sputum samples, 1 mL of media for swab samples.

### B Principle of Operation:
These components of the media are intended to inactivate SARS CoV-2 capsids, disrupt/lyse lipid membranes, denatures proteins, inactivates enzymes, and stabilize SARS CoV-2 RNA. The transport device is designed for storage of specimens between 68-77 °F (20-25 °C) for 28 days. Do not mix with sodium hypochlorite. The media contains the following reagents:

- Inactivation buffer
- Salts
- pH buffer
- Water

Please refer to the MSDS or SDS sheet for safety specifics regarding the chemical composition. and

1. Quality Control:
   N/A

## 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):** | K202641 | DEN170029 |
|---|---|---|
| Device Trade Name | DNA/RNA Shield Collection Tube | PrimeStore MTM |
| **General Device Characteristic Similarities** | Transport device for the stabilization of microbial nucleic acids | Transport device for the stabilization of microbial nucleic acids |
| Intended Use/Indications For Use | The DNA/RNA Shield™ collection tube is intended for the stabilization and inactivation of upper and lower respiratory human specimens suspected of containing SARS-CoV-2. These devices can be used for collection transport and storage of specimens at ambient temperatures (20-25°C). Specimens collected and stored in a DNA/RNA Shield™ collection tube are suitable for use with legally marketed molecular diagnostic devices. | 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. |
| Inactivation | RNA sample | RNA samples |
| Storage Temperature 20-25°C | SARS-CoV-2 RNA: 28 days | MTB DNA 36 days:<br>Flu A RNA 8 days |
| Sample source | Human respiratory | Human respiratory |
| **General Device Characteristic Differences** | | |
| Specimen Stability at 2-4 | No 2-4°C claim | ≤ 8 days flu<br>≤ 36 days MTB |
| Analyte | RNA | RNA and DNA |
| Specimen Type | Lower, Upper Respiratory and saliva Specimens for SARS-CoV-2. | Nasal wash suspected of containing Influenza A virus. Sputum samples suspected of containing MTB. |

## VI Standards/Guidance Documents Referenced:

Special controls that are applicable to regulation 21 CFR 866.2950.

## 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 DNA/RNA Shield Collection tube with media is 24 months after the date of manufacture. The stability of the DNA/RNA Shield Collection tube with media was performed using Realtime and Accelerated stability on a total of 6 lots. Stability looked for bacterial and fungal growth in the media along with properties of the media, appearance, pH, voltage resistance and density.

   **Sterilization:** The DNA/RNA Shield Collection tube with media are not sold as sterile nor are they intended to be sterilized by the user. These vials are single use devices that do not require cleaning by the operator. 24 month sterility testing demonstrated no growth detected up to and beyond this claimed time point.

6. Detection Limit:

   a) Limit of Detection (LoD) testing was conducted to determine the lowest concentration of whole genome (Genome equivalent copies (GEC)) that contains measurable nucleic acids and that can be repeatedly recovered from the transport media with a greater than 95% accuracy. GEC were used because of safety concerns during the COVID-19 pandemic. Nucleic acid detection was then validated on the EUA Authorized Quick SARS-CoV-2 rRT-PCR Kit assay to establish a concentration of nucleic acid which will form the basis of additional testing. (Testing near the LoD for the additional studies will challenge the

DNA/RNA Shield Collection media to preserve nucleic acids from degradation under a variety of stage conditions.)

b) LoD testing was initially performed by spiking multiple concentrations of GEC of SARS-CoV-2 into clinically negative matrix (sputum or OP swab). Each sample matrix was prepared and tested individually. The media/matrices were spiked with the following concentrations of GEC of SARS-CoV-2 to achieve final concertation of 250 GEC/mL, 167 GEC/mL, 83 GEC/mL and 0 GEC/mL. The final concentration of each spiked media/matrix was then extracted using an automated or manual extraction using the Quick RNA MagBead Kit using the KingFisher Flex Purification System for automated extraction. Amplification was conducted on the Authorized Quick SARS-CoV-2 2rRT-PCR Kit.

The study objective was to determine the detectable GEC of SARS-CoV-2 after spiking into media/sputum. No detection (Ct = 40) was observed at a concentration of < 83 GEC/mL. All other higher concentrations demonstrated some recovery of SARS-Cov-2 RNA. A second confirmatory LoD testing was conducted at a concentration of 250 GEC/mL (15 GEC/reaction) for both sputum and oral swabs. Each sample type was further tested using automated and manual extraction. 250 GEC/mL (15 GEC/reaction) was replicated 20 times for both sputum and oral swabs using automated and manual extraction techniques. The same detection testing scheme and concentration ranges was reported in the Authorization of the Quick SARS-CoV-2 2rRT-PCR Kit.

In summary the LoD testing at 250 GEC/mL (15 GEC/reaction) resulted in 20/20 replicates for automated extraction and 19/20 replicates for manual extraction for sputum and 19/20 replicates for automated extraction and 19/20 replicates for manual extraction for oral swabs. These results at a concentration of 250 GEC/mL (15 GEC/reaction) meet the pre-defined acceptance criteria for all both sample matrices, sputum and swab.

c) Stability

Stability studies evaluated the stability of SARS-CoV-2 at 1250 GEC/mL spiked into each of the two matrices, sputum and oral swabs. Clinically negative matrices were added to media and spiked with GEC of SARS-CoV-2. The samples were then tested immediately to establish a time point zero and then stored at room temperature (20-25°C, 68-77° F) for 28 days. Amplification was conducted on the Authorized Quick SARS-CoV-2 assay and used to determine stability GEC of SARS-CoV-2. The stability study analyzed a total of 2 lots of DNA/RNA Shield Collection tubes; two tubes from each lot were tested totaling 4 replicates tested at each time point and for each temperature range. An initial time point designated as Day 0 and was included as the initial Ct average. Ten additional testing time points were performed at Day 1, 2,3,4,5,6,7,14,21, and 28 for ambient temperature (20-25°C, 68-77°F) for both sputum and swab studies.

A pre-defined acceptance criteria of (+/-) 3.0 Ct from time zero was used to establish stability and preservation of nucleic acids (RNA from SARS-CoV-2) as determined by real-time PCR, for 20-25°C and without loss of detection signal using statistical analysis.

Stability testing of RNA from SARS-CoV-2 GEC spiked into clinically negative sputum and swabs stored at 20-25°C resulted in a maximum variation of 2.4 $C_t$ over 28 days. The results demonstrated acceptable RNA stabilization at 20-25°C over a four week period.

d) Inactivation

SARS-CoV-2 ($9x10^5$ PFU) was spiked into DNA/RNA Shield media (at a ratio of 1:3). The virus and media were then serially diluted and added to the cell culture media and incubated on the cell mono layer for 1 hour. SARS-CoV-2 only and DNA/RNA Shield media only were also incubated accordingly to serve as internal controls. 2 days after the one hour exposure the veroE6 cell monolayer was fixed with 10% formaldehyde and stained with 0.5% crystal violet to enable plaque visualization and enumeration. Wells that were not stained demonstrated the cytopathic effect (CPE) of the virus. The dilution of the virus or inactivated virus that caused CPE was recorded.

Inactivation rate:

The DNA/RNA Shield media showed no cytotoxicity on veroE6 cells when a 1:1,000 dilution factor was applied to the DNA/RNA Shield media. The 1:1,000 dilution factor is needed to avoid cytotoxic effects. The mixture of SARS-CoV-2 and DNA/RNA Shield media combined for 30 minutes demonstrated at least a 2 log reduction in SARS-CoV-2 after a 30 min exposure. Greater than a 2 log reduction of SARS-CoV-2 could not be quantified based on the starting concentration of the virus compounded by the fact that viral CPE could not be observed at < 3.0 logs due to cellular destruction by DNA/RNA Shield media.

Specimens must be used at a ratio of no more than 1:1 specimen to media and held at a minimum of 30 minutes to achieve inactivation of SARS-CoV-2.

7. 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.