June 26, 2024

Hangzhou Bioer Technology Co., Ltd
℅ Hanson Chen
Official Correspondent
Shenzhen Joyantech Consulting Co., Ltd
1713A, 17th Floor, Block A, Zhongguan Times Square,
Nanshan District
Shenzhen, Guangdong GD755, China

Re: K222771
Trade/Device Name: Sample Preservative Fluid
Regulation Number: 21 CFR 866.2950
Regulation Name: Microbial Nucleic Acid Storage And Stabilization Device
Regulatory Class: Class II
Product Code: QBD
Dated: July 25, 2022
Received: September 14, 2022

Dear Hanson Chen:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Noel J. Gerald -S

Noel J. Gerald, Ph.D.
Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K222771

Device Name
Sample Preservative Fluid

Indications for Use *(Describe)*
The Sample Preservative Fluid is intended for the stabilization, transportation, and inactivation of infectious, unprocessed, upper respiratory specimens suspected of containing Influenza A virus. Specimens transported in the Sample Preservative Fluid are stable refrigerated (2-8°C) and at room temperature (20-25°C). The Sample Preservative Fluid is suitable for use with compatible legally marketed molecular diagnostic devices.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

1. Submission Sponsor

Applicant Name	HANGZHOU BIOER TECHNOLOGY CO.,LTD
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Date Prepared	June 24, 2024

Consultant information

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2. Device information

Trade name	Sample Preservative Fluid
Common name	Sample Preservative Fluid
Model	BSC82X1-A1
Classification	II
Classification name	Microbial Nucleic Acid Storage And Stabilization Device
Product code	QBD
Regulation No.	21 CFR 866.2950

3. Legally Marketed Predicate Device

Trade Name	PrimeStore MTM
510(k) Number	DEN170029
Product Code	QBD
Manufacturer	Longhorn Vaccines and Diagnostics, LLC

4. Device Description:

Sample Preservative Fluid is a medium for stabilization of Influenza A RNA during sample transport/storage. The fluid is composed of guanidine thiocyanate, Triton X-100, and nuclease-free water. Sample Preservative Fluid is provided in a labeled screw-cap tube.

Sample Preservative Fluid configuration:

- BSC82X1-A1: a screw-cap tube filled with 2 mL of Sample Preservative Fluid liquid and a prepackaged nasopharyngeal swab for sample collection
- Nasopharyngeal swab: regular size, sterile disposable sample swab (80mm breakpoint)

5. Intended Use/Indication for Use:

The Sample Preservative Fluid is intended for the stabilization, transportation, and inactivation of infectious, unprocessed, upper respiratory specimens suspected of containing Influenza A virus. Specimens transported in the Sample Preservative Fluid are stable refrigerated (2-8°C) and at room temperature (20-25°C). The Sample Preservative Fluid is suitable for use with compatible legally marketed molecular diagnostic devices.

6. Substantial Equivalence Comparison:

	Device: K222771	**Predicate: DEN170029**
Device Trade Name	Sample Preservative Fluid	PrimeStore MTM
General Device Characteristic Similarities		
Intended Use / Indications For Use	The Sample Preservative Fluid is intended for the stabilization, transportation, and inactivation of infectious, unprocessed, upper respiratory specimens suspected of containing Influenza A virus. Specimens transported in the Sample Preservative Fluid are stable refrigerated (2-8°C) and at room temperature (20-25°C). The Sample Preservative Fluid is suitable for use with compatible 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.
Specimen storage temperature	2-25 °C	2-25 °C
Shelf-life	24 months	24 months
General Device Characteristic Differences		
Microorganism nucleic acids preserved	Influenza A virus	Influenza A virus and Mycobacterium tuberculosis
Specimen type	Upper respiratory specimens	Nasal washes and sputum samples
Analyte	RNA	DNA, RNA
Specimen stability	2-25 °C ≤ 35 days	For Influenza A virus: 4 °C ≤ 29 days 27 °C ≤ 8 days

7. Non-clinical Testing

7.1 Shelf-life:

Three lots of Sample Preservative Fluid stored at 2-8°C and 25°C were assessed at 10 timepoints (0, 3, 6, 12, 13, 15, 18, 21, and 24 months). At each timepoint, each kit was evaluated for bacterial or fungal growth, changes in appearance, the tightness of the cap to ensure no leakage, and density of the liquid.

Acceptance criteria: There should be no bacterial or fungal growth, no obvious change in appearance, no tube leakage at -0.08 MPa for ten minutes, and a media density of 1.06 ± 0.04 g/mL.

All three lots stored at 2-8°C and 25°C met physical and chemical property evaluation acceptance criteria for all timepoints. There was no bacterial or fungal growth, change in appearance, no leakage, and no change in density over time. The shelf-life of the reagent when stored at 2-25°C is 24 months.

The Sample Preservative Fluid is not claimed to be sterile nor is it intended to be sterilized by the end user. These vials are single-use devices. The products are packaged in sterile PE bags to ensure the media is not contaminated during shipping.

7.2 Detection Limit:

Limit of detection (LoD) testing was conducted to evaluate the lowest concentration of analyte that can be detected at greater than or equal to 95% detection rate.

Preliminary Limit of Detection (LoD):

The cleared assay used to determine the LoD was the Cepheid Xpert Xpress Flu/RSV Assay (K180218) when testing samples collected in the subject device. The LoD of the Xpert Xpress Flu/RSV Assay for Influenza A H3N2 is:

- Influenza A/Perth/16/2009: 0.01 $TCID_{50}$/mL
- Influenza A/Victoria/361/2011: 0.75 $TCID_{50}$/mL

Because the two viral strains used in the Cepheid LoD study were no longer available, another Influenza A H3N2 strain, A/California/2/2014 VR-1938, was used.

Influenza A H3N2 (A/California/2/2014, VR-1938) was diluted with negative nasal matrix to 0.32 $TCID_{50}$/mL. Serial two-fold dilutions were performed to create samples at 0.16, 0.08, 0.04, 0.02 and 0.01 $TCID_{50}$/mL. Five replicates of each sample were tested for Influenza A with the Xpert Express Flu/RSV Assay, table 1 below. The lowest concentration that yielded a greater than or equal to 80% detection rate was further tested to confirm LoD.

Table 1. Preliminary LoD test results:

Influenza A Concentration ($TCID_{50}$/mL)	Rep 1 (Ct)	Rep 2 (Ct)	Rep 3 (Ct)	Rep 4 (Ct)	Rep 5 (Ct)	Avg (Ct)	SD (Ct)	CV (%)	Detection Rate (%)
0.32	33.4	33.1	34.2	33.2	33.4	33.5	0.39	1.16%	100%
0.16	34.3	34.5	36.9	34.2	34.3	34.8	1.03	2.97%	100%
0.08	35.0	36.1	35.3	35.2	34.5	35.2	0.519	1.47%	100%
0.04	37.3	36.2	39.2	36.8	No Ct	37.4	1.12	3.01%	80%
0.02	38.5	38.7	38.3	No Ct	No Ct	38.5	0.163	0.424%	60%

0.01	37.9	37.3	No Ct	No Ct	No Ct	37.6	0.300	0.798%	40%

Confirmatory Limit of Detection (LoD):
To confirm LoD, additional testing of 20 replicates at 0.04 $TCID_{50}$/mL was performed. When testing of 8 replicates at 0.04 $TCID_{50}$/mL yielded >2 negative results, testing was terminated and a retest was performed at 0.08 $TCID_{50}$/mL. 100% of replicates at 0.08 $TCID_{50}$/mL were positive confirming the assay LoD as 0.08 $TCID_{50}$/mL, table 2 below.

Table 2. Confirmatory LoD test results:

Replicate	0.08 $TCID_{50}$/mL Influenza A (Ct)
1	34.5
2	35.2
3	36.2
4	35.2
5	35.0
6	35.1
7	36.5
8	35.4
9	35.6
10	35.1
11	35.2
12	35.8
13	34.8
14	35.2
15	35.3
16	36.4
17	35.1
18	35.2
19	35.6
20	34.7
Average	35.4
SD	0.517
CV (%)	1.46%
Detection Rate (%)	100%

7.3 Specimen stability:
A specimen stability study was conducted to evaluate the stability of Influenza A virus RNA spiked into negative matrix and stored in Sample Preservative Fluid at a refrigerated temperature (2-4°C) and room temperature (20-25°C) for 35 days. Influenza A H3N2 (A/California/2/2014, VR-1938) was diluted to 3x the LoD (0.24 $TCID_{50}$/mL) with negative nasal matrix collected with three reagent lots. Samples collected with each of the three lots were tested in replicates of four with the Xpert Xpress Flu/RSV Assay on Day 0. Samples were stored at refrigerated (2-4°C, table 3 below) and room temperature (20-25°C, table 4 below). Samples were tested in replicates of four on Days 1, 8, 15, 22, and 35.

Table 3. Influenza A stability 2-4°C:

Specimen	Lot	Rep	Day0 (Ct)	Day1 (Ct)	Day8 (Ct)	Day15 (Ct)	Day22 (Ct)	Day35 (Ct)

0.24 $TCID_{50}$/mL Influenza A in nasal matrix	1	1	33.5	33.1	33.4	33.9	33.6	35.6
		2	33.5	34.0	33.7	34.0	33.9	34.3
		3	33.0	33.4	33.4	33.5	34.3	33.9
		4	33.4	34.8	33.9	33.3	33.9	34.0
	2	1	33.4	33.2	33.5	33.8	33.5	34.3
		2	34.0	33.4	33.4	33.9	34.0	34.4
		3	33.5	33.5	33.9	33.7	33.5	34.1
		4	33.9	33.3	33.8	33.5	34.0	33.7
	3	1	33.7	33.6	33.8	33.5	33.8	34.2
		2	33.7	33.3	33.7	33.6	33.8	33.7
		3	33.5	33.2	34.0	33.6	33.7	34.2
		4	33.3	33.5	33.7	33.7	33.7	34.4
	Average		33.5	33.5	33.7	33.7	33.8	34.2
	SD		0.256	0.446	0.203	0.197	0.222	0.473
	CV		0.764%	1.33%	0.604%	0.586%	0.655%	1.38%

Table 4. Influenza A stability 20-25°C:

Specimen	Lot	Rep	Day0 (Ct)	Day1 (Ct)	Day8 (Ct)	Day15 (Ct)	Day22 (Ct)	Day35 (Ct)
0.24 $TCID_{50}$/mL Influenza A in nasal matrix	1	1	34.0	34.1	34.3	33.6	33.4	33.9
		2	34.0	33.9	33.3	33.9	33.9	34.7
		3	33.7	33.3	34.0	33.9	33.9	34.1
		4	33.5	33.9	34.3	34.2	33.7	34.4
	2	1	33.8	33.3	33.6	33.5	33.6	34.0
		2	33.9	33.2	33.4	34.0	34.0	33.4
		3	33.4	33.4	34.5	33.4	33.9	33.7
		4	33.7	33.5	33.4	33.6	33.4	34.1
	3	1	34.0	33.4	33.6	33.3	33.7	34.1
		2	33.5	33.0	33.7	34.3	34.0	35.2
		3	34.0	33.5	33.8	34.2	33.6	34.2
		4	34.3	33.1	33.6	34.1	33.7	34.0
	Average		33.8	33.5	33.8	33.8	33.7	34.2
	SD		0.254	0.325	0.379	0.180	0.201	0.443
	CV		0.752%	0.971%	1.12%	0.534%	0.597%	1.30%

At each timepoint, Influenza A spiked into nasal matrix and preserved at refrigerated temperature (2-4°C) or room temperature (20-25°C) yielded positive results, which showed the Influenza A H3N2 nucleic acid was detected.

All the Ct values fell within a 3.0 Ct range of results from the Ct values generated for time point zero, which met the pre-defined acceptance criteria. The Influenza A H3N2 virus nucleic acid was preserved in the Sample Preservative Fluid without degradation at refrigeration (2-4°C) and room (20-25°C) temperatures for 35 days.

8. Viral Inactivation Study:
An inactivation study was performed to determine the rate the Sample Preservative Fluid

inactivates Influenza A.

Cytotoxicity Study:
A cytotoxicity study was performed to determine at what dilution ratio the Sample Preservative Fluid would not be toxic to a cell monolayer.

A preliminary test was performed by diluting the Sample Preservative Fluid with complete cell culture medium at multiple dilutions (from 1:10 up to 1:8000) and adding it to a monolayer of cells. When the Sample Preservative Fluid dilution ratio exceeded 1:4000 both the test group and the control group showed normal cell morphology and growth, demonstrating that there was no significant cytotoxicity for the Sample Preservative Fluid with high dilution ratios.

A confirmatory test was performed by diluting the Sample Preservative Fluid with complete cell culture medium at multiple dilution (from 1:1000 to 1:10000) and adding it to a monolayer of cells. When the dilution ratio reached or exceeded 1:3500, both the test group and the control group showed normal cell morphology and growth status, and no significant difference between the test group and the control group were observed.

When the dilution ratio reached or exceeded 1:3500, both the test group and the control group showed normal cell morphology and growth status, and no significant difference between the test group and the control group were observed. There was no toxicity to the MDCK cell monolayer when the Sample Preservative Fluid was diluted to equal to or greater than 3500 times.

Inactivation Study:
To evaluate successful inactivation of Influenza A virus, Influenza A H3N2 virus was combined at a ratio of 1:1 in negative nasal matrix mixed with Sample Preservative Fluid and incubated for 30 and 60 seconds. The initial concentration of the Influenza A H3N2 was $>1x10^7$ $TCID_{50}$/mL. Each mixture was then diluted 3500x (determined in the cytotoxicity study) with complete cell culture medium. Each dilution was plated into 8 wells of a 96-well cell culture plate in triplicate and incubated for 3-4 hours. The medium was removed and replaced with 100µL of complete cell culture medium. The plate was incubated at 34°C and 5% atmosphere for 4-7 days. The plate was observed for cytopathic effects and virus titers were calculated.

Additionally, positive controls containing Influenza A H3N2 virus and sterile saline were mixed at a ratio of 1:1 and incubated for 30 and 60 seconds. Each mixture was then diluted to 3500x (determined in the cytotoxicity study) with complete cell culture medium. Each dilution was plated into 8 wells of a 96-well cell culture plate in triplicate and incubated for 3-4 hours. The medium was removed and replaced with 100µL of complete cell culture medium. The plate was incubated at 34°C and 5% CO_2 atmosphere for 4-7 days. The plate was observed for cytopathic effects and virus titers were calculated.

Negative controls were also evaluated as part of this study in which MDCK cells were incubated with complete cell culture medium 34°C and 5% CO_2 atmosphere for 4-7 days. The plate was observed for cell growth and culture contamination.

No cytotoxicity was observed in the cell monolayer after exposure to Influenza A virus samples incubated in Sample Preservative Fluid for 30 or 60 seconds. The result was ≥4.7 logarithmic reduction in Influenza A after 30 and 60 seconds in the Sample Preservative Fluid. Therefore, the Sample Preservative Fluid inactivated Influenza A H3N2 in MDCK cells and the device demonstrated viral inactivation of >99.99%. Cytotoxicity was observed in the positive control group, and no viral infection was observed in the negative control group.

9. Conclusions:

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