September 28, 2023

Zymo Research
Julie Ogi
Regulatory Office
17062 Murphy Ave
Irvine, California 92614

Re: K231013
Trade/Device Name: DNA/RNA Shield SafeCollect Saliva Collection Kit
Regulation Number: 21 CFR 866.2950
Regulation Name: Microbial nucleic acid storage and stabilization device
Regulatory Class: Class II
Product Code: QBD
Dated: August 15, 2023
Received: August 29, 2023

Dear Julie Ogi:

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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K231013

Device Name
DNA/RNA Shield™ SafeCollect Saliva Collection Kit

Indications for Use *(Describe)*
The DNA/RNA Shield™ SafeCollect Saliva Collection Kit is intended for the collection, inactivation, stabilization, and transportation, of unprocessed saliva specimens suspected of containing SARS-CoV-2. The DNA/RNA Shield™ SafeCollect Saliva Collection Kit is intended to transport and store saliva specimens at ambient temperature (20-25°C) from the collection site to the laboratory. Specimens collected and preserved in a DNA/RNA Shield™ SafeCollect Saliva Collection kit sample collection tube are suitable for use with 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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Applicant	Zymo Research 17062 Murphy Ave. Irvine, CA 92614 USA
Establishment Registration No.	3007020052
Contact Person	Julie Ogi Regulatory Officer Phone (949) 679-1190 Fax (949) 266-9452 e-mail jogi@zymoresearch.com
Summary Date	March 31, 2023
Proprietary Name	DNA/RNA Shield™ SafeCollect Saliva Collection Kit
US Product Codes / Regulation Numbers	QBD - Transport device for the stabilization of microbial nucleic acids / 21 CRF 866.2950
Classification	Class II
Predicate Device	DNA/RNA Shield™ Collection Tube (K202641)

Intended Use

The DNA/RNA Shield SafeCollect Saliva Collection Kit is intended for the collection, inactivation, stabilization, and transportation, of unprocessed saliva specimens suspected of containing SARS-CoV-2. The DNA/RNA Shield SafeCollect Saliva Collection Kit is intended to transport and store saliva specimens at ambient temperature (20-25°C) from the collection site to the laboratory. Specimens collected and preserved in a DNA/RNA Shield SafeCollect Saliva Collection kit sample collection tube are suitable for use with legally marketed molecular diagnostic devices.

Device Description

The DNA/RNA Shield SafeCollect Saliva Tube 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 (20-25 °C) and is intended to inactivate SARS-CoV-2, effectively lyses cells from collected saliva specimens.

The DNA/RNA Shield SafeCollect Saliva Tube contains a foil seal barrier that sequesters the DNA/RNA Shield transport media inside of the tube, until the cap, with a Safe Puncture tip is used to seal the DNA/RNA Shield SafeCollect Saliva tube. When the foil seal barrier is broken by the Safe Puncture Tip, the specimen is then, and only then mixed with the DNA/RNA Shield™ transport media.

The DNA/RNA Shield SafeCollect Saliva Collection Kit consists of a DNA/RNA Shield SafeCollect Saliva Tube, a funnel designed for the collection of human saliva samples, and a cap with a Safe Puncture tip. Sample collection is conducted under the supervision of a healthcare provider. The user deposits their saliva into the collection tube with the aid of the attached funnel, the user removes the funnel and replaces it with the cap. Upon twisting and closing the Safe Puncture tip cap, the DNA/RNA Shield is released into the tube and mixes with the saliva.

Comparison to Predicate Device

Device & Predicate Device(s):	Device: K231013	Predicate K202641
Device Trade Name	DNA/RNA Shield SafeCollect Saliva Collection Kit	DNA/RNA Shield Collection Tube
General Device Characteristic Similarities		
Intended Use/Indications For Use	The DNA/RNA Shield SafeCollect Saliva Collection Kit is intended for the collection, inactivation, stabilization, and transportation, of unprocessed saliva specimens suspected of containing SARS-CoV-2. The DNA/RNA Shield SafeCollect Saliva Collection Kit is intended to transport and store saliva specimens at ambient temperature (20-25°C) from the collection site to the laboratory. Specimens collected and preserved in a DNA/RNA Shield™ SafeCollect Saliva Collection kit sample collection tube are suitable for use with legally marketed molecular diagnostic devices.	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.
Analyte	SARS-CoV-2 RNA	Same
Sample stability	20-25°C	Same
Collection media	DNA/RNA Shield media	Same
Special conditions for use	For prescription use only For *in-vitro* diagnostic use only	Same
General Device Characteristic Differences		
Sample collection	Saliva	Upper and lower respiratory specimens
RNA Stabilization at room temperature	Saliva: up to 21 days	Upper/lower respiratory tract samples: up to 28 days

Performance data

a) Detection Limit:

An analytical sensitivity study was conducted to determine the Limit of Detection (LoD) of SARS-CoV-2 when detected in saliva samples collected using the DNA/RNA Shield SafeCollect Saliva Collection kit in combination with the authorized Quick SARS-CoV-2 rRT-PCR Kit for SARS-CoV-2 detection. To determine a preliminary LoD, SARS-CoV-2 negative saliva was used as a clinical matrix collected in DNA/RNA Shield SafeCollect Saliva Collection Kit and spiked with inactivated SARS-CoV-2. The preliminary LoD was determined as the lowest concentration for which 5/5 independent replicates tested positive. Results for the preliminary LoD determination are shown in Table 1 below.

Table 1: Preliminary LoD Determination

Concentrations Tested (GEC/mL)	Replicates	SARS-CoV-2 Targets	Interpretation	Call Rate
8.3×10^4 (5,000 GEC/rxn)	1	27.33	Positive	5/5
	2	28.03	Positive	
	3	27.73	Positive	
	4	27.60	Positive	
	5	27.73	Positive	
8.3×10^3 (500 GEC/rxn)	1	29.77	Positive	5/5
	2	28.83	Positive	
	3	29.33	Positive	
	4	29.64	Positive	
	5	29.97	Positive	
8.3×10^2 (50 GEC/rxn)	1	32.37	Positive	5/5
	2	32.95	Positive	
	3	32.31	Positive	
	4	32.88	Positive	
	5	32.49	Positive	
83 (5 GEC/rxn)	1	39.54	Positive	5/5
	2	34.16	Positive	
	3	38.87	Positive	
	4	32.54	Positive	
	5	33.36	Positive	
8.3 (0.5 GEC/rxn)	1	N/A	Negative	1/5
	2	44.00	Inconclusive	
	3	37.89	Positive	
	4	40.94	Inconclusive	
	5	N/A	Negative	

To confirm the LoD, inactivated SARS-CoV-2 was spiked into negative saliva specimens and 20 replicates were independently processed. The lowest concentration at which all 5 replicates were positive in the preliminary LoD (i.e., 83 GEC/mL) was used as a starting point for the confirmatory LoD study. Therefore, concentrations above 83 GEC/mL (increasing by factor 2) were tested until ≥ 19/20 replicates tested positive. The final LoD for saliva was determined to be at the lowest concentration at which ≥ 19/20 replicates test positive. The final LoD was determined to be 250 GEC/mL (15 GEC/rxn). Results of the confirmatory LoD study for saliva specimens can be seen in Table 2 below.

Table 2: Confirmatory LoD Determination

Concentrations Tested (GEC/mL)	Replicates	SARS-CoV-2 Targets	Interpretation	Call Rate
250 (15 GEC/ rxn)	1	34.62	Positive	19/20
	2	34.83	Positive	
	3	33.99	Positive	
	4	N/A	Negative	
	5	35.84	Positive	
	6	33.94	Positive	
	7	35.25	Positive	
	8	35.01	Positive	
	9	33.99	Positive	
	10	33.69	Positive	
	11	34.01	Positive	
	12	34.03	Positive	
	13	35.32	Positive	
	14	34.46	Positive	
	15	35.84	Positive	
	16	35.56	Positive	
	17	33.76	Positive	
	18	35.33	Positive	
	19	34.00	Positive	
	20	33.56	Positive	
166 (10 GEC/ rxn)	1	35.57	Positive	17/20
	2	35.35	Positive	
	3	35.78	Positive	
	4	N/A	Negative	
	5	33.80	Positive	
	6	34.42	Positive	
	7	35.19	Positive	
	8	35.01	Positive	
	9	34.87	Positive	
	10	36.17	Positive	
	11	N/A	Negative	
	12	34.25	Positive	
	13	37.80	Positive	
	14	N/A	Negative	
	15	34.64	Positive	
	16	35.44	Positive	
	17	35.51	Positive	
	18	35.46	Positive	
	19	36.05	Positive	
	20	34.66	Positive	
83 (5 GEC/ rxn)	1	41.48	Inconclusive	13/20
	2	37.02	Positive	
	3	37.57	Positive	
	4	37.07	Positive	
	5	N/A	Negative	
	6	36.54	Positive	
	7	37.17	Positive	
	8	37.25	Positive	

	9	35.21	Positive	
	10	N/A	Negative	
	11	37.08	Positive	
	12	N/A	Negative	
	13	35.57	Positive	
	14	N/A	Negative	
	15	N/A	Negative	
	16	N/A	Negative	
	17	34.74	Positive	
	18	35.01	Positive	
	19	35.03	Positive	
	20	35.54	Positive	

Conclusion:
The DNA/RNA Shield SafeCollect medium used to collect saliva, and the Authorized Quick SARS-CoV-2 2rRT-PCR Kit reached a SARS-CoV-2 LoD of 250 GEC/mL (15 GEC/reaction) for saliva specimens, which is equivalent to the established LoD of the authorized reference assay.

b) Stability of SARS-CoV-2 in saliva specimens:
The room temperature (20-25 ºC) stability of SARS-CoV-2 in DNA/RNA Shield SafeCollect Saliva kit was established by spiking 3X LoD of SARS-CoV-2 (750 GEC/ml) (see LoD section above) into negative saliva specimens collected using the DNA/RNA Shield SafeCollect Saliva Collection Kit and stored at room temperature in a time course study of 21 days. The room temperature stability of SARS-CoV-2 was measured using the Quick SARS-CoV-2 rRT-PCR Kit at day 0, 1, 2, 3, 4, 5, 6, 7, 14, and 21. Results are summarized in Table 3

Table 3. SARS-CoV-2 Stability

Concentration Tested	Days at Room Temperature	Replicates	Average Ct (Standard Deviation)	Call Rate
Low Positive 3x LoD (750 GEC/mL)	Day 0	3	33.75 (0.21)	3/3
	Day 1	3	33.37 (0.22)	3/3
	Day 2	3	34.10 (0.35)	3/3
	Day 3	3	33.93 (0.32)	3/3
	Day 4	3	34.24 (0.97)	3/3
	Day 5	3	34.34 (0.24)	3/3
	Day 6	3	34.75 (0.87)	3/3
	Day 7	3	34.44 (0.41)	3/3
	Day 14	3	33.98 (0.36)	3/3
	Day 21	3	34.05 (0.48)	3/3

Conclusion:
There is no significant change in stability over time and the data are within the acceptance criteria (≤+/-10% deviation from day 0). Stability is determined by acceptable data that supports the stability claim and does not exceed day 0 by a 3-log range. Therefore, SARS-CoV-2 is stable in saliva specimens collected using the DNA/RNA Shield SafeCollect Saliva Collection kit for up to 21 days when stored at room temperature (20-25 ºC).

c) Inactivation:

An inactivation study was conducted to test DNA/RNA Shield SafeCollect Saliva Collection kit media ability to inactivate SARS-CoV-2. The inactivation study used a stock titer of $9x10^5$ PFU/mL for SARS-CoV-2. The study was performed in a Biosafety Level 3 (BSL-3) facility.

Stock SARS-CoV-2 was spiked into DNA/RNA Shield media (at a ratio of 1:3 using 100 µL of viral stock was

mixed with 300 µL of DNA/RNA Shield SafeCollect medium). The virus and media mixture were incubated for 30 mins at room temperature. The mixture was then serial diluted in cell culture medium and added to confluent monolayers of VeroE6 cells. Cells and media were incubated at 37°C in 5% CO2 for one hour with gentle rocking every 15 minutes. Media was aspired and 1.0 mL of pre-warmed overlay media was added. Cells were incubated for two days, fixed in 10% formaldehyde, and stained with 0.5% crystal violet to enable plaque visualization and enumeration. A positive control (untreated viral stock) and negative control (media only) were included in each run. A no-virus media control (DNA/RNA Shield media only) was also included to assess whether the media was cytotoxic. The study was replicated three independent times.

Inactivation rate:
The DNA/RNA Shield media showed no cytotoxicity on veroE6 cells when the media was diluted 1:1,000 with cell culture media. The 1:1,000 dilution factor is needed to avoid cytotoxic effects the DNA/RNA Shield media has on the cell monolayer. 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. 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 need to dilute the DNA/RNA Shield media 1:1000. CPE could not be observed at < 3.0 logs due to the cytotoxic effects of the DNA/RNA Shield media.

Conclusion:
Zymo DNA/RNA shield inactivates SARS-CoV2 when incubated for at least 30 minutes at room temperature.

Based on the above, Zymo Research believes that the DNA/RNA Shield SafeCollect Saliva Collection kit is substantially equivalent to the commercially distributed product DNA/RNA Shield Collection Tube for the transport, inactivation, LoD and stabilization of saliva, specimens suspected of containing SARS-CoV-2. No new issues of safety or effectiveness were found for the DNA/RNA Shield Collection Tube.