EMERGENCY USE AUTHORIZATION (EUA) SUMMARY FOR THE SALIVADIRECT AT-HOME COLLECTION KIT

For *In vitro* Diagnostic Use
Rx Only
For use under Emergency Use Authorization (EUA) only
For individuals 18 years or older

INTENDED USE

The SalivaDirect At-Home Collection Kit is intended for use by individuals aged 18 years and older including individuals without symptoms or other reasons to suspect COVID-19 to self-collect saliva specimens at home, unsupervised, when determined by a healthcare provider to be appropriate. Specimens collected using the SalivaDirect At-Home Collection Kit can be transported at ambient temperature for testing at an authorized laboratory. SARS-CoV-2 RNA from the saliva specimen is maintained in the specimen packaging and is only for use in molecular diagnostic testing performed using an in vitro diagnostic (IVD) test for the detection of SARS-CoV-2 that is indicated for use with the SalivaDirect At-Home Collection Kit.

Testing is limited to laboratories designated by Yale School of Public Health Department of Epidemiology of Microbial Diseases, that includes the Clinical Molecular Diagnostics Laboratory, Department of Pathology, Yale School of Medicine, located at 310 Cedar St., New Haven, CT 06510, certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, that meet requirements to perform high complexity tests.

The SalivaDirect At-Home Collection Kit is only for use under the Food and Drug Administration's Emergency Use Authorization.

SPECIAL CONDITIONS OF USE STATEMENTS

For Emergency Use Authorization (EUA) only.
For prescription use only.
For in vitro diagnostic use only.
For professional use only.
For individuals 18 years or older.

The SalivaDirect At-Home Collection Kit is only authorized for use in conjunction with an in vitro diagnostic (IVD) test for the detection of SARS-CoV-2 that has been issued an EUA and is authorized for use with this collection kit.

DEVICE DESCRIPTION AND TEST PRINCIPLE

The SalivaDirect At-Home Collection Kit consists of a saliva collection device (either a Funnel or Bulb Pipette), sterile plastic collection tube, biohazard bag, absorbent sheet, alcohol pad, return shipping box, instructions for use, patient identifier sticker, activation card, UN 3373 Pak, and return label.

REAGENTS AND MATERIALS

Components supplied with the home collection kit include:

Table 1. SalivaDirect At-Home Collection Kit (5 mL tube + Funnel)

Supplier	Product	Product Number
Medline	Round collection funnel, Sterile, 500/bg, 4000/cs	Kingston Mfg KICFUNNEL
Thomas Scientific	Empty Nest 5.0mL Tube with Concave-Convex Cap	20A00M344
Thomas Scientific	3x5 Biohazard Bags	1150H29
Thomas Scientific	3x3 Absorbent Sheets	1233R56
Thomas Scientific	Alcohol Prep Pad	2904T41
ULINE	6 x 7" 1 Mil Poly Bags	S-10869
Federal Industries	Box - 9x6x2	
ALOM	Date of Birth Sticker	
ALOM	Activation Card	
ALOM	Instructions for Use	
ALOM	Collection Brochure	
FedEx or UPS	UN 3373 Pak (FedEx) or Category B Pak (UPS)	
Lab Fulfillment Center	Return Label	
Apollo Renal Therapeutics (DBA - Artemis Plastics)	Artemis	V-2021-5
Ningbo Dasky Life Science	Dasky	8011923

Table 2. SalivaDirect At-Home Collection Kit (1 mL tube + Bulb Pipette)

Supplier	Product	Product Number
VWR	disposable individually wrapped pipettes	76285-390
Hamilton	1.0 mL Internal thread with Lid	SDR-096-03
Thomas Scientific	3x5 Biohazard Bags	1150H29
Thomas Scientific	3x3 Absorbent Sheets	1233R56
Thomas Scientific	Alcohol Prep Pad	2904T41
ULINE	6 x 7" 1 Mil Poly Bags	S-10869
Federal Industries	Box - 8x6x1	
ALOM	Date of Birth Sticker	
ALOM	Activation Card	
ALOM	Instructions for Use	
ALOM	Collection Brochure	
FedEx or UPS	UN 3373 Pak (FedEx) or Category B Pak (UPS)	

Lab Fulfillment Center	Return Label	

Home Collection Kit Ordering and Processing:

Individuals may request the SalivaDirect At-Home Collection Kit via one of two workflows:

1. The individual is screened for testing eligibility by their healthcare professional (HCP). The Authorized Laboratory does not provide a questionnaire to determine eligibility for COVID testing, since this is left to the ordering HCP to consider appropriate guidelines in determining the best treatment for their patient. After HCP determination of testing eligibility, the HCP places a test order with the Authorized Laboratory for their patient. The HCP provides the patient's address to the Authorized Laboratory. The Authorized Laboratory (via a fulfillment center) ships the SalivaDirect At-Home Collection Kit to the individual suspected of COVID-19, as determined to be appropriate by the HCP.
2. Alternatively, the individual can request a test on the Authorized Laboratory's website and complete a required health COVID-19 questionnaire via a secure online portal (based on current CDC testing guidelines). An HCP from an independent physician organization contracted by the Authorized Laboratory (e.g., PWN) will review the individual response to the questionnaire, determine eligibility, and issue an order for the SalivaDirect At-Home Collection Kit as appropriate. The Authorized Laboratory (via a fulfillment center) ships the SalivaDirect At-Home Collection Kit to the individual suspected of COVID-19 as determined to be appropriate by the HCP. Individuals exhibiting severe COVID warning symptoms should seek emergency medical care.

The individual deemed to be appropriate for testing receives the SalivaDirect At-Home Collection Kit and proceeds with unsupervised saliva collection following the Instructions for Use (IFU) provided inside the kit, and ships the sample to an Authorized SalivaDirect Laboratory.

The SalivaDirect At-Home Collection Kit collects virus RNA in a saliva specimen; it can also be used for the transportation and short-term room temperature storage of a sample. The SalivaDirect At-Home Collection Kit is a non-invasive alternative for collecting viral RNA by/from individuals who are suspected of COVID-19 by their healthcare provider for use with a SARS-CoV-2 test authorized for use with the SalivaDirect At-Home Collection Kit.

The SalivaDirect At-Home Collection Kit includes one of two saliva collection devices: a Funnel with a 5 mL transport tube, or a Bulb Pipette with a 1 mL transport tube.
The kit also includes a biohazard specimen bag with absorbent material, alcohol prep pad, patient identifier sticker, activation card, return box and pre-labeled FedEx UN 3373 Pak or UPS Category B Pak along with Instructions for Use and Collection Brochure.

After opening the SalivaDirect At-Home Collection Kit containing the Funnel and 5 mL transport tube, the patient is first instructed to activate their kit online at the Authorized Laboratory's website, following the instructions on the web page to fill in the necessary registration information and sample collection date and time. Next, the patient is instructed to pick up the funnel and tube, and swallow once to clear their mouth. Then, the patient holds the funnel up so that it surrounds their mouth, then gently release the saliva that has collected in their

mouth into the funnel. The patient is instructed to collect enough saliva, so the tube is half-filled. The patient repeats the same process until the tube is half-full. Once the patient has collected enough saliva, they are instructed to remove the funnel from the sample tube and tightly screw the cap back onto the tube. The patient then uses the alcohol wipe to wipe their hands and the sample tube, then places the closed sample tube into the biospecimen bag. Finally, the patient is instructed to drop off the sealed collected specimen at a FedEx or UPS drop off location on the same day it was collected.

After opening the SalivaDirect At-Home Collection Kit containing the Bulb Pipette and 1 mL transport tube, the patient is first instructed to activate their kit online at the Authorized Laboratory's website, following the instructions on the web page to fill in the necessary registration information and sample collection date and time. Next, the patient is instructed to swallow once to clear their mouth, then pick up the bulb pipette and press the bulb end between their index finger and thumb to push out all the air. The patient is then instructed to keep their lips mostly closed and insert the tip of the bulb pipette into their mouth where saliva is collecting. Then they are instructed to release their finger and thumb to allow the bulb pipette to fill with saliva, then remove the bulb pipette from their mouth and pick up the sample tube with their other hand. The patient is then instructed to insert the tip of the bulb pipette into the sample tube, then gently push down on the bulb to slowly empty the saliva into the tube. The patient repeats these steps until the sample tube is about half filled. Once the patient has collected enough saliva, they are instructed to tightly screw the cap back onto the sample tube. The patient then uses the alcohol wipe to wipe their hands and the sample tube, then places the closed sample tube into the biospecimen bag. Finally, the patient is instructed to drop off the sealed specimen at a FedEx or UPS drop off location on the same day it was collected.

The SalivaDirect At-Home Collection Kit Instructions for Use provides an outline of the kit handling procedures, the self-collection process, and step-by-step instructions to ship samples on the same day of collection for next day delivery to the laboratory. Specimens are shipped at ambient temperature and received at the clinical laboratory for testing with the SalivaDirect test within 56 hours of sample collection.

Test results are provided to the ordering health care provider and the patient via secure email and/or online portal. An HCP will directly contact individuals with positive or invalid/inconclusive test results. In addition, a link to the fact sheets for both HCP and patient for the test is included in the test report that goes back to the patient via the online portal.

INSPECTION OF SPECIMENS

Specimens received at the clinical laboratory authorized for testing specimens collected using the SalivaDirect At-Home Collection Kit undergo the following accessioning prior to acceptance for testing:

- Date of shipment received must be less than or equal to 56 hours from the time of sample collection
- Tubes that are leaking, open, damaged or empty are rejected
- Tubes with missing or damaged identifiers are rejected
- Non-SalivaDirect tubes are rejected

CONTROLS TO BE USED WITH THE SARS-COV-2 ASSAY

Specimen Collection Control:
Sample collection control will be monitored by the detection of the human sample control, RNase P, to determine that an acceptable sample was collected by the user. Alternatively, sample collection visually observed by a healthcare provider through a telemedicine visit could also serve as this control.

The following controls (at a minimum) should be included in the in vitro diagnostic (IVD) molecular test for the detection of SARS-CoV-2 RNA that is indicated for use with saliva specimens collected with the SalivaDirect At-Home Collection kit:

1. A negative (no template) control is needed to eliminate the possibility of sample contamination and is used on every assay plate.
2. A negative extraction control is needed to eliminate the possibility of sample contamination during nucleic acid extraction and is used with every extraction run.
3. A positive template control is needed to verify that the assay run is performing as intended and is used on every assay plate
4. An internal control targeting RNase P is needed to verify that nucleic acid is present in every sample and is used for every sample processed. This ensures that saliva of a sufficient quantity and quality was tested.

PERFORMANCE EVALUATION

1) SalivaDirect At-home Collection Kit Shipping Stability Studies:

To evaluate the stability of SARS-CoV-2 RNA detection by the SalivaDirect test when collected using the SalivaDirect At-Home Collection kit, a simulated shipping study was performed. The sample stability study was designed to evaluate the effect of temperature variation on the stability of SARS-CoV-2 RNA detection following transport of saliva specimens in the saliva collection tubes of the SalivaDirect At-Home Collection Kit. The shipping study simulated shipping at temperature conditions that could be experienced during the summer and winter months. Tables 3 and 4 detail the summer and winter thermal profiles evaluated in this study.

Table 3: Summer Profile*

Temperature	Cycle Period	Cycle Period Hours	Total Time Hours
40°C	1	8	8
RT (19-20°C)	2	4	12
40°C	3	2	14
28°C	4	36	50

40°C	5	6	56

Table 4. Winter Profile*

Temperature	Cycle Period	Cycle Period Hours	Total Time Hours
-20°C	1	8	8
RT (19-20°C)	2	4	12
-20°C	3	2	14
4°C	4	36	50
-20°C	5	6	56

*Shipping conditions for cycle periods 2 through 5 are modeled after ISTA 7D 2007 shipping standard (48-hour domestic freight transport) where for cycle period 3 and 5 the temperature has been increased from 35°C to 40°C. The cycle period 1 (8 hours) has been included for the time delay between collection of the sample and shipment of the sample. The remaining time (48 hours) covers the domestic shipment within the continental U.S. Cycle periods are sequential with the "cycle period hours" required per cycle listed in the table. After each cycle period, the "total time hours" increments by the number of hours in the cycle period.

For these sample stability studies, a positive saliva specimen from a confirmed COVID-19 healthcare worker with a known virus concentration (3.7×10^4 copies/µL) was spiked into saliva collected from healthcare workers who tested negative for SARS-CoV-2 using the CDC assay. Stability of SARS-CoV-2 detection was determined in 10 weakly positive specimens spiked at 2x LoD (12 copies/µL) and 20 moderate positive specimens spiked at 8x LoD (50 copies/µL) through the two different temperature profiles before testing with the SalivaDirect test; following the temperature profiles, samples were treated with the ThermoFisher Scientific proteinase K and tested with the NEB Luna (2x) RT-qPCR kit on the Bio-Rad CFX96 Touch.

Ten out of 10 weak positive samples (100%) and 20/20 moderate positive samples (100%) were positive after the summer and winter temperature cycles. On average, N1 Ct values remained within 3.0 Cts as compared to when tested fresh, indicating acceptable specimen stability under the tested conditions. A summary of the mean Ct values obtained is provided in Table 5.

Table 5. Shipping stability

Concentration	Condition	n	Average Ct N1	Average Ct RP
50 copies/µL	Fresh (t=0h)	20	33.66	27.60
	Summer (t=56h)	20	31.44	29.00
	Winter (t=56h)	20	33.23	27.41
12 copies/µL	Fresh (t=0)	10	35.67	26.46
	Summer (t=56h)	10	36.45	29.76
	Winter (t=56h)	10	35.47	27.42

2) <u>Human Usability Studies for the SalivaDirect At-Home Collection kit</u>

A total of 60 participants between the ages of 19 and 81 years who represented a range of racial and educational backgrounds were enrolled in this study to evaluate the usability of the SalivaDirect At-Home Collection Kit for mailing a saliva sample to a CLIA-certified lab for SARS-CoV-2 testing by the SalivaDirect test. Further study demographics are presented below:

Category	n (%)	Funnel (n=31)	Bulb Pipette (n=29)
Sex			
Male	28 (46)	14 (45)	14 (48)
Female	32 (54)	17 (55)	15 (52)
Age			
18-29	13 (21)	7 (23)	6 (21)
30-39	28 (46)	11 (35)	16 (16)
40-49	5 (8)	4 (13)	1 (3)
50-59	5 (8)	3 (10)	2 (7)
60-69	5 (9)	4 (13)	2 (7)
70+	4 (7)	2 (6)	2 (7)
Education			
High School/GED	14 (25)	9 (29)	6 (21)
Bachelors	22 (36)	11 (35)	10 (34)
Masters	10 (16)	7 (23)	4 (14)
PhD/MD	14 (23)	4 (13)	9 (31)
Race			
Black/African American	10 (16)	6 (19)	4 (14)

Category	n (%)	Funnel (n=31)	Bulb Pipette (n=29)
Hispanic/Latino	10 (16)	5 (16)	5 (17)
Asian/South Asian	8 (13)	4 (13)	3 (10)
White	32 (54)	16 (52)	17 (59)
Native American	0	0	0

Once informed consent was provided via an online form, selected study participants were alerted by a brief email and shipped a SalivaDirect At-Home Collection Kit containing either a Funnel or a Bulb Pipette via FedEx. A total of 31 individuals were evaluated for use with the Funnel, and 29 individuals were evaluated for use with the Bulb Pipette. There was minimal contact with study participants to replicate the official ordering process as closely as possible. Following the Instructions for Use in the SalivaDirect At-Home Collection Kit, participants self-collected a saliva sample and returned this to the Yale School of Public Health for testing by the SalivaDirect test. Participants completed a survey about their experience following the collection, scoring responses on a scale of 1 (strongly disagree) to 5 (strongly agree). All of the samples (n = 60) were tested for SARS-CoV-2 using the SalivaDirect test. A laboratory survey assessing the sample quality was completed by the technician during testing.

Study participants reported understanding the instructions and 100% understood that they could not eat/drink/smoke prior to collecting the sample. Results regarding the sample collection, compiled from all 60 participants, are summarized below:

Collection feed-back (1 = strongly disagree, 5 = strongly agree)	Average	SD	%
I read all of the instructions	4.59	1.12	91.80
I understood all of the instructions	4.39	1.13	90.16
I knew what to do if I had any questions	3.61	1.52	73.77
Did the instructions clearly describe how to collect the sample?	4.67	1.11	91.80
Did you understand that you could not eat/drink/smoke prior to collecting the sample	5.00	0.00	100.00
Did you understand that eating/drinking/smoking prior to collecting the sample might get false results	4.54	1.29	88.52

When looking at responses for each collection device type (funnel or bulb pipette), responses remained similar and are summarized below:

Collection device feed-back (1 = strongly disagree, 5 = strongly agree)	Funnel	Bulb Pipette
I read all of the instructions	4.62	4.55
I understood all of the instructions	4.48	4.26
I knew what to do if I had any questions	4.00	3.35
Did the instructions clearly describe how to collect the sample?	4.59	4.74

Collection device feed-back (1 = strongly disagree, 5 = strongly agree)	**Funnel**	**Bulb Pipette**
Did you understand that you could not eat/drink/smoke prior to collecting the sample	5.00	5.00
Did you understand that eating/drinking/smoking prior to collecting the sample might get false results	4.45	4.61
I knew how much saliva to put in the tube	4.45	4.84
It was easy to put the appropriate amount of saliva into the tube	3.69	3.90
I feel confident that I collected the sample properly	4.41	4.58
I needed help collecting the sample	1.28	1.26
Sample collection was difficult	1.90	1.87
Sample collection was comfortable	4.14	4.48
Did you get any saliva on the outside of the collection tube	1.69	2.03
Did you know what to do if saliva came into contact with the outside of the collection tube?	3.34	3.84
Did you understand that if you did not follow the procedure exactly, you might geta false result?	4.59	4.74

The internal control, human RNaseP was detected in 100% of the samples collected with each of the devices, indicating an adequate specimen was collected. Laboratory survey responses confirmed that 100% of the samples were easy to pipette and of sufficient volume. No sample tested positive for SARS-CoV-2. Results for the questions in the laboratory survey are summarized below:

Lab questions (1 = strongly disagree, 5 = strongly agree)	**Funnel**	**Bulb Pipette**	**Average**
The sample was of sufficient volume (200-500 ul)	5.0	4.0	4.50
The sample was easy to pipette	4.8	5.0	4.91
The sample was normal, true saliva	4.8	5.0	4.89
The sample was free from food particles	5.0	5.0	5.00
The sample was not unusually discolored	4.9	5.0	4.95
The sample tested positive for human RNase P	5.0	5.0	5.00
The sample tested positive for SARS-CoV-2	0.0	0.0	0
If the sample tested positive for SARS-CoV-2, this was reported back to the study participant	NA	NA	NA

The results from this study demonstrate that users are able to comprehend the instructions for both of the SalivaDirect At-Home Collection Kits as well as collect an adequate specimen for SARS-CoV-2 testing with the SalivaDirect test.

Warnings

- This product has not been FDA cleared or approved, but has been authorized for emergency use by FDA under an EUA;

- This product has been authorized only for the collection and maintenance of saliva specimens as an aid in the detection of nucleic acid from SARS-CoV-2, not for any other viruses or pathogens;
- The emergency use of this product is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of medical devices under Section 564(b)(1) of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 360bbb-3(b)(1), unless the declaration is terminated or authorization is revoked sooner.