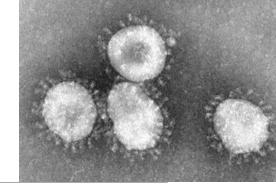


Objectives

- 1. Review the types of swabs used for sample collection for SARS-CoV-2.
- 2. Briefly discuss the quality procedures required for medical swab manufacturing.
- 3. Review the types of transport media used for SARS-CoV-2 sample collection.
- 4. Understand the factors which make up a good specimen collection.
- 5. Understand the evolution of collection swabs and transport media recommendations by the FDA during the COVID19 epidemic.



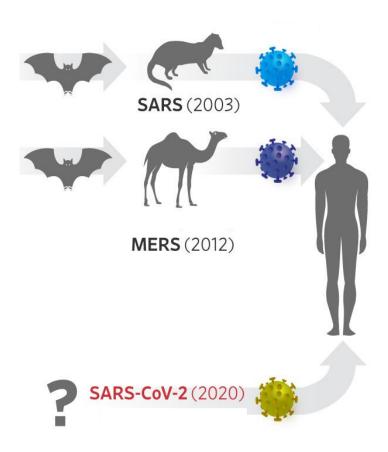
Coronavirus

General Description

- ss RNA genome, helical capsid, an envelope
- Name comes from solar coronal pattern of spikes in envelope seen on EM
- 2nd major group or viruses causing "common cold"; outbreaks occur from December to March
- Symptoms begin 2 days after infection & peak 2 days later
- Transmission by aerosol and direct contact; asymptomatic inf. = 50%
- One strain predominates during outbreak; reinfections are common

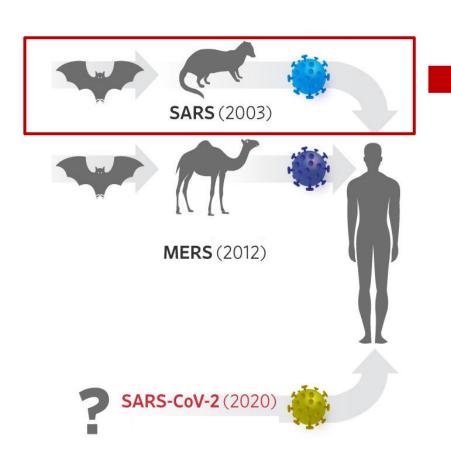
CoV Epidemic Potential

Coronaviruses are jumping increasingly from animals to humans, creating new threats



Epidemic Potential

Coronaviruses are jumping increasingly from animals to humans, creating new threats



SARS – Sudden Acute Respiratory Syndrome

SARS-CoV

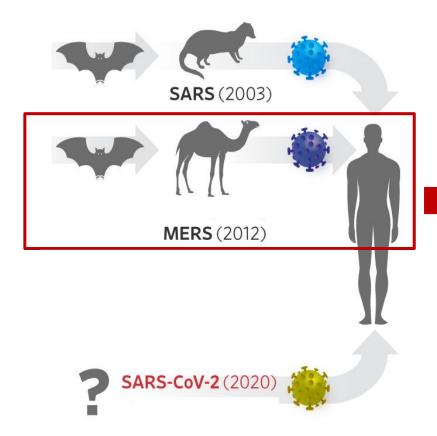
atypical pneumonia → high fever, chills, malaise, mortality ~10%

2002 outbreak – believed that the virus jumped species from bats to animals raised for food (civet cat; racoon dog) to man in China

8300 cases - 785 deaths

Epidemic Potential

Coronaviruses are jumping increasingly from animals to humans, creating new threats



MERS – Middle Eastern Respiratory Syndrome (MERS-CoV)

Saudi Arabia in 2012

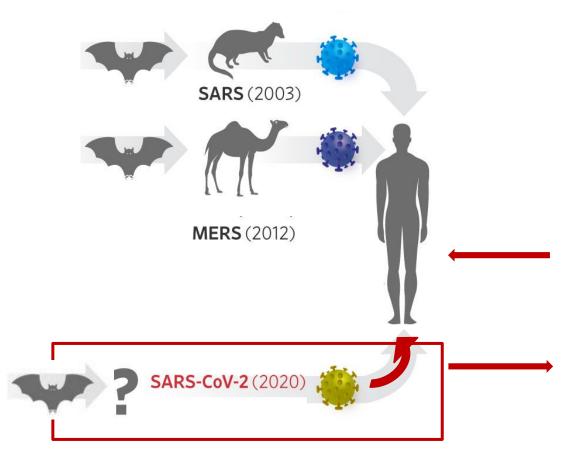
- severe acute respiratory illness, fever, cough, SOB
- bats → camels → humans
- 2,494 cases of MERS-CoV infection and nearly 900 deaths have been documented.
- ~ 30% fatality

MERS in the U.S.

- > May 2014, MERS was confirmed in the U.S. in 2 travelers from Saudi Arabia
- > CDC recognizes the potential for MERS-CoV to spread & cause more cases in the U.S. and globally
- > Information provided for travelers
- > Health departments, hospitals, & clinicians prepared

Epidemic Potential

Coronaviruses are jumping increasingly from animals to humans, creating new threats



Sudden Acute Respiratory Syndrome SARS-CoV-2

pangolin

The only known mammals to have large, protective keratin scales covering their skin.

Sought after for ethnomedicine.

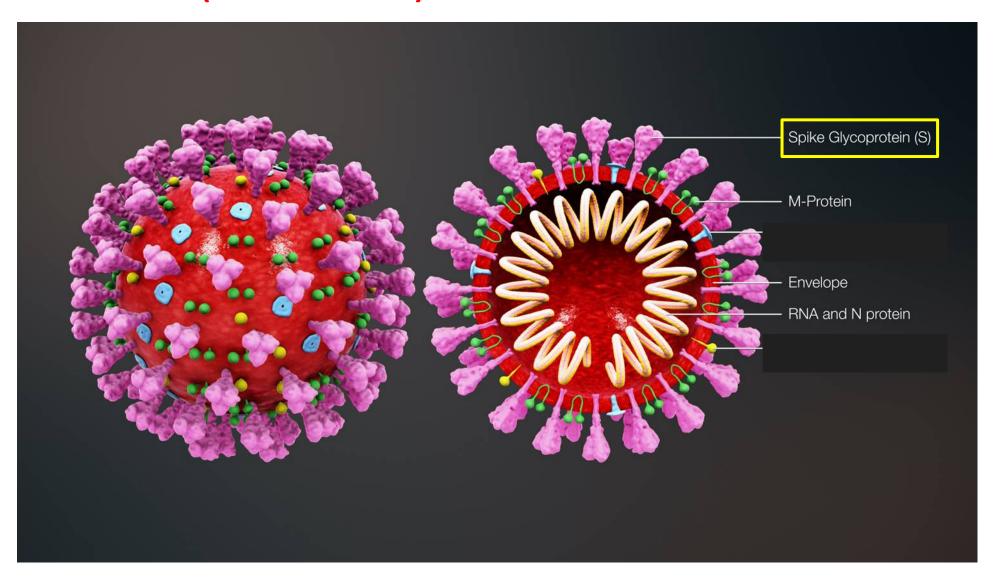
Origin: Wuhan China

Open air "wet market"

7

- Probably originated from bats
- -Virus jumped from animals to humans in China late last year
- -Possibly from a market selling exotic animals for meat

SARS-CoV-2 (2019nCoV) = virus COVID19 = disease



Infectivity

- Transmission occurs primarily via respiratory droplets/coughs & sneezes (range ~6').
- It is thought the virus reaches peak respiratory load sometime during the 1st week of symptoms then declines.
- "Pre-symptomatic shedding"
 - Patients can shed a large amount of virus 2-3 days <u>before symptoms</u>.
 - A substantial proportion of transmission probably occurs via this route.
- Indirect contact via contaminated surfaces.
- The virus is inactivated by soap, alcohol, heat, bleach, disinfectants; all which destabilizes the lipid bilayer of its envelope.

Transmissibility: R₀ ("r naught")

Average # of people that will get the infection from 1 infected person

If R₀ < 1, each existing infection causes less than one new infection; the disease will decline and eventually die out.

If R₀ = 1, each existing infection causes one new infection; the disease will stay alive and stable, but there won't be an outbreak or an epidemic.

If R₀ > 1, each existing infection causes more than one new infection; the disease will be transmitted between people, and there may be an outbreak or epidemic.

R₀ only applies when everyone in a population is susceptible to the disease.

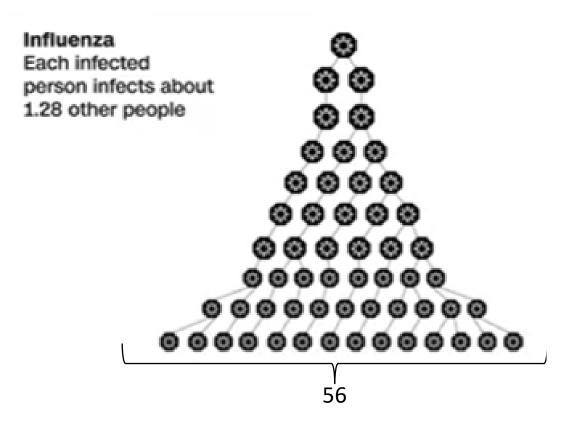
This means:

No one has been vaccinated

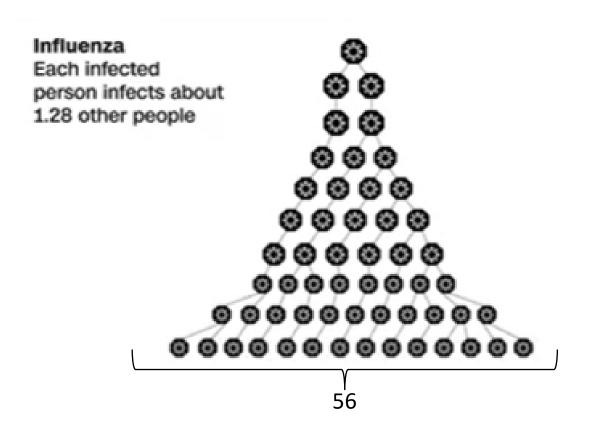
No one has had the disease before

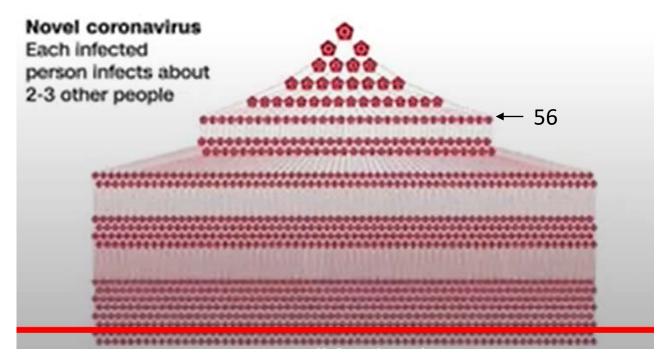
There's no way to effectively control the spread of the disease

10 generations of infection

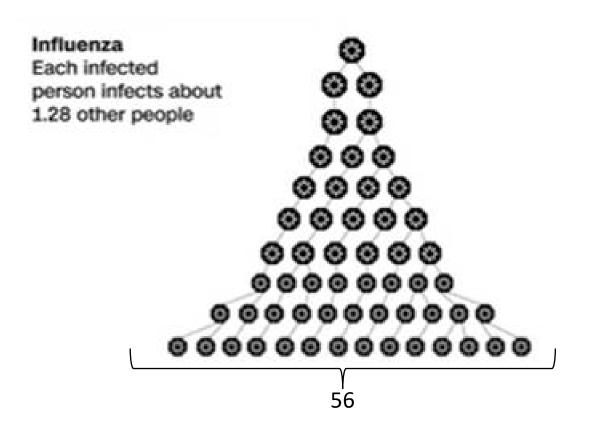


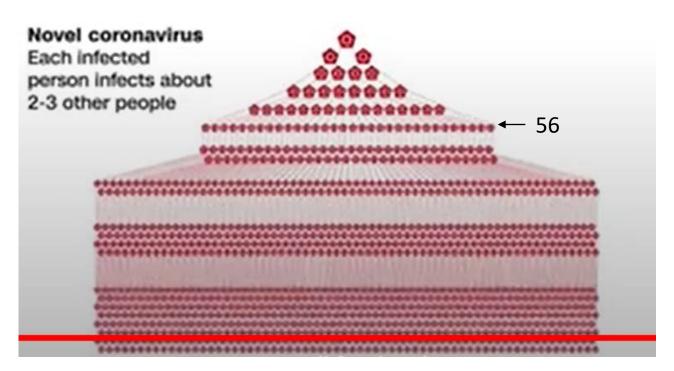
10 generations of infection





10 generations of infection





Mitigation

Specimen Collection





Home Food

Drugs

Medical Devices

Radiation-Emitting Products

Vaccines, Blood & Biologics

Animal & Veterinary

Cosmetics

Tobacco Products

Establishment Registration & Device Listing

FDA Home Medical Devices Databases

New Search





1 result found for Establishment Registration

or Business Trade Name : COPAN

Establishment Registration or FEI Number:

2436875

Establishment Name	Registration Number	Current Registration Yr 2020	
COPAN DIAGNOSTICS, INC. CA/USA	2436875		
 Equipment, Laboratory, General Purpose, Lab BD Inoculation Loops; Disposable Transfer Pi Loops; Hardy SpeedStreakers; HealthLink Inc Inoculation Loops; Inoculation Needles; Inocu Pipettes; Troy Biologicals Loops And Needles 	Manufacturer; Repackager/Relabeler		
 Kit, Quality Control For Culture Media - CryoE 	ank	Repackager/Relabeler	
 Micro Pipette - ACT Transfer Pipettes; AeroMo Transfer Pipettes 	Manufacturer		
 Culture Media, Non-Propagating Transport - E 	Repackager/Relabeler		
 Device, Specimen Collection - BD FecalSwab 	Repackager/Relabeler		
Applicator, Absorbent Tipped, Sterile - Buccal Sterile; FLOQBrush; FLOQSwab; Foam Swab Sterile; Polyester Fiber Swab, Sterile; Rayon	Manufacturer		



Class 1 Device Requirements

Analytical Studies

- a. Testing performed on product post-sterilization to ensure biocompatibility (verified to be non-cytotoxic, non-irritating, and non-sensitizing) for limited contact.
- b. Studies demonstrate effective performance for **mechanical properties**, flexibility, durability after sterilization including tensile testing, torsional testing, and flexural testing.
- c. Needs to show equivalent performance for adequate collection of specimen from nasal, nasopharyngeal, oropharyngeal, etc. sites.



Sterilization, Packaging and Labeling

The **sterilization** process is validated by the manufacturer prior to distribution including the bioburden testing of final product.

Packaging must address seal strength and packaging integrity for shipping.

Swabs would be **labeled** appropriately for their intended use, including the site it is intended to sample [e.g. nasal, nasopharyngeal, etc.).

Labeling will include:

- A description of the material and its characteristics.
- Recommendations to sufficiently reduce any potential risks for use.

Examples:

- 1) a caution against use of non-sterile product, and
- 2) recommendations for to visually inspect products for physical integrity prior to use.



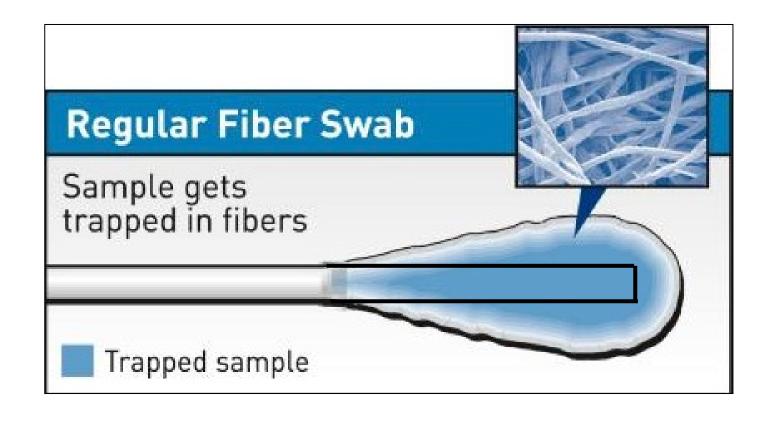
Relevant Guidance Documents and Standards

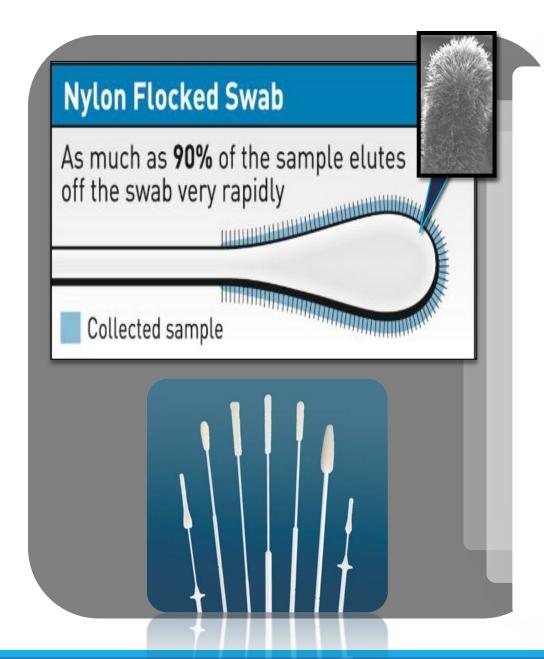
ISO 13485:2016 Medical devices -- Quality management system

ISO 10993-1:2018 Biological evaluation of medical devices

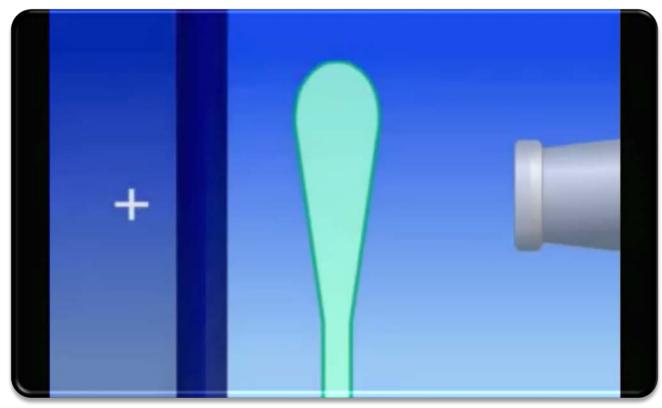
Traditional Fiber Wrapped Swabs







Flocked Swab vs. Traditional Swab



Traditional Fiber Swab Sample diffuses and becomes trapped in the fiber mattress



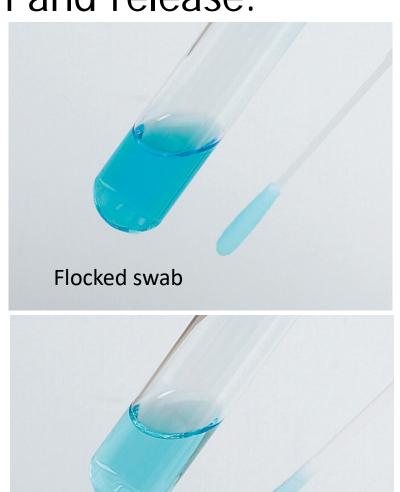
Flocked Swab
Liquid sample
stays close to
the surface
and elutes out
rapidly and

spontaneously

Velvet brush-like texture efficiently dislodges and collects infected respiratory epithelial cells

Flocked Swabs improve specimen absorption and release.

Spun fiber swab



Type of Swab	Average Sample Absorption Volume	Average Sample Release Volume (vortexing)		
Regular Fiber Wrapped (Rayon/Dacron)	105μL	35μL (or 33%)		
Regular Foam	36μL	33μL (or 92%)		
Regular Flocked	131μL	127μL (or 97%)		
Minitip Fiber Wrapped (Rayon/Dacron)	45μL	45μL		
Minitip Foam	23μL	21μL (or 90%)		
Minitip Flocked	94μL	92μL (or 98%)		

Absorption and elution volumes

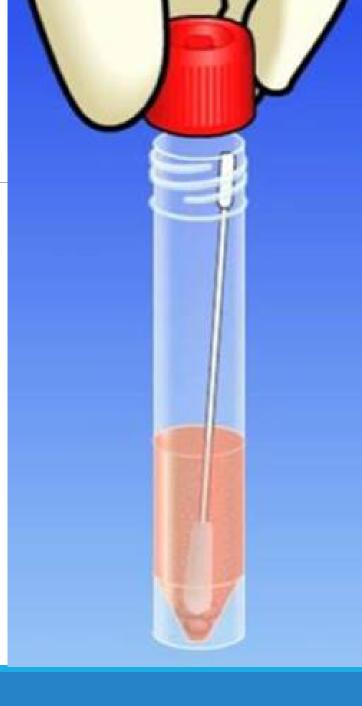
	Average Sample Absorption Volume	Average Sample Release Volume (vortexing)		
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Minitip Fiber Wrapped (Rayon/Dacron)	45μL	45μL		
Minitip Foam	23μL	21μL (or 90%)		
→ Minitip Flocked	94μL	92μL (or 98%)		

Absorption and elution volumes

Transport Media

Samples collected and transferred into preservation medium:

- Viral Transport Media (VTM or UTM™): Viruses, Chlamydia, Mycoplasma, Ureaplasma
- Amies: Routine bacteriology
- NA Stabilization Media: General microbiology molecular testing



Viral Transport Media

UTM™ Universal Transport Medium

FDA cleared collection and transport system suitable for collection, transport (48 hrs @ RT/4C), maintenance and long-term freeze storage of clinical specimens.

An open platform that can be used for:

Culture

EIA

DFA

NAAT

Paired with Flocked swabs = equivalent to nasal aspirates and nasal washes for the diagnosis of respiratory virus infections.



AMIES Liquid Media

ESwab™

Liquid Based Collection and Transport System for Microbiology Samples

Flocked swab + 1mL of Liquid Amies in a plastic, screw cap tube.

Collection and transport device for aerobic, anaerobic, and fastidious bacteria for up to 48 hours.



NA Stabilization Media

Guanidine-thiocyanate based medium which stabilizes RNA and DNA

A Guanidine-thiocyanate based medium that stabilizes RNA and DNA of viruses, bacteria.

Ensures preservation of RNA and DNA at room temperature for weeks or months (if frozen).

Inactivates microbial viability allowing safe specimen handling.



NA Stabilization Media

Guanidine-thiocyanate based medium which stabilizes RNA and DNA

FDA NOTE: This transport media contains guanidine thiocyanate which produces a dangerous chemical reaction releasing cyanide gas when exposed to bleach.

WARNING:

Do not use PrimeStore MTM with the Hologic Panther or Panther Fusion Systems due to a disinfecting step involving bleach that is specific to the platform.

O When the bleach interacts with the guanidine thiocyanate in the transport media, it produces dangerous cyanide gas.



On February 29, 2020, the FDA issued new guidance for the development of COVID-19 molecular diagnostic tests.

 Kit manufacturers and Laboratory LDTs are required to submit an EAU to the FDA within 15 business days after their validation is complete and distribution/testing has started.



- **CDC assay** issued 1st EUA on 2/4/20:
 - NP swabs & OP swabs (nylon or polyester) / VTM
 - Additional swabs types, collections sites, and transport materials were authorized by the FDA thereafter.

TIMELINE: Collections/sites authorized by the FDA

		February 29	March 23	April 3	April 14	May 6
Overview		Healthcare workers can take NP / OP swabs in facility CDC assay (2/4/20)	Individuals can self- collect samples in facility with foam nasal swab	All swabs can be stored in normal saline as alternative transport media	Polyester swabs can be used for nasal collection with expanded supply	Self-collected nasal swab using spun polyester in dry tube, with no cold chain for up to 3 days
	Specimen collector	HCW	HCW, Self	HCW, Self	HCW, Self	HCW, Self
	Specimen sites/swabs	NP, OP (HCW only)	NP, OP (HCW only) MT (Flocked), Nasal	NP, OP (HCW only) MT (Flocked), Nasal	NP, OP (HCW only) MT (Flocked), Nasal	NP, OP (HCW only) MT (Flocked), Nasal
	Nasal swab materials		Foam	Foam	Foam Polyester, Rayon	Foam, Spun Polyester, Rayon
Components authorized by FDA	Transport media	VTM Added: 1 st - liquid Amies 2 nd - PBS	VTM liquid Amies PBS	VTM liquid Amies PBS Normal saline	VTM liquid Amies PBS Normal saline NA media	VTM liquid Amies PBS Normal saline NA media Dry
	Physical testing site	Healthcare facility or drive-thru	Healthcare facility or drive-thru	Healthcare facility or drive-thru	Healthcare facility or drive-thru	Healthcare facility, drive-thru, Home Collection



COVID19 - Specimen collection

FDA believes that a <u>flocked nasopharyngeal specimen</u> is the preferred choice for swab-based SARS-CoV-2 testing.

If a flocked nasopharyngeal specimen is not available, then any of the following are acceptable:

- Oropharyngeal (throat) specimen collected by a healthcare professional (HCP)
- Mid-turbinate specimen by onsite self-collection or HCP (using a flocked tapered swab)
- Anterior nares specimen by onsite self-collection or HCP (using a foam or spun polyester/rayon swab)

Swab education Norman Sharples 051120

https://www.nejm.org/doi/full/10.1056/NEJMvcm2010260#full

Studies forming FDA guidance

(supported by The Gates Foundation)

Study	Purpose	Site of Collection	Swab Type	Transport Media	Clinical Site	Laboratory	Study outcome		
	Evaluate self-collection, from alternative sites	Nasopharyngeal Nasal Mid-turbinate	Comparator Foam Flocked nylon	VTM	Everett Clinic/UHG	Quest Diagnostics	 Self-collected nasal specimen equivalent to NP by healthcare worker 94% Self-collected MT specimen equivalent to NP by healthcare worker 96% 		
		Tongue dorsum	Flocked nylon				 Self-collected tongue specimen equivalent to NP by healthcare worker < 90% 		
	Evaluate self-collection,	Oropharyngeal	Comparator	.,	Stanford	Stanford Clinical Virology Lab	Nasal swab, collected by health	hcare worker,	
Stanford	from nasal passage	Nasal	Foam	VTM			equivalent to OPNasal swab, self-collected, equ	uivalent to OP	
	Evaluate alternative polyester swab	Nasal	Foam	VTM Saline	Everett Clinic/UHG	Quantigen	Polyester swab is equivalent to foam nasal swab		
			Polyester				with VTM (foam may be slightly more sensitive at very low viral concentration) • Polyester swab is equivalent to foam nasal swab with saline (foam may be slightly more sensitive at very low viral concentration)		
Everett			Foam						
Clinic #2	Evaluate alternative transport media		Polyester						
	Evaluate variable heat stability of virus on foam and polyester swab in saline and dry conditions		Foam	Dry	N/A	Quantigen		100	
		Nasal Polyes					3	32C 40C	
Quantigen # 1							Foam-dry 80	0 hr 12 hr	
			Polyester	Saline			Polyester-dry 80	0 hr 12 hr	
				Sallile			Polyester-saline 56	6 hr 12 hr	

Additional studies

Study	Purpose	Site of Collection	Swab Type	Transport Media	Clinical Site	Laboratory	Study outcome
Quest	Evaluated stability of virus RNA in specimen transport media at various storage conditions	NP/ OP / sputum/BAL with spiked sample	various	UTM M4 ESwab saline	N/A	Quest Diagnostics	 All spiked samples - in all transport media: Ct values were stable from -30°C to 25°C for 7-10 days ¹
		Mid-		VTM	Home		Preliminary results demonstrated that dry swabs would support
Seattle	Evaluated dry swabs	turbinate	Flocked	Dry	collection kits	UW	that dry swabs would support detection of SARS-CoV-2 without impacting sensitivity

¹ https://jcm.asm.org/content/jcm/early/2020/04/23/JCM.00708-20.full.pdf

HOME COLLECTION

Example:



Self-collection of anterior nares specimen, at home or in community setting



Spun polyester swab, foam swab



Swab placed in dry tube or in saline

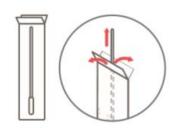


Sent to the lab in the mail*



Remove the nasal swab from the wrapper by pulling the two ends of the wrapper apart (like you would to open a band-aid).

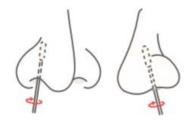
Be careful to only touch the handle, not the tip.



2 Swab nose

Gently insert the **entire** soft tip of the swab into one nostril until you feel a bit of resistance and rub it in a circle around your nostril **4 times**.

Next, gently insert **the same swab** into the other nostril and rub it around the same way.

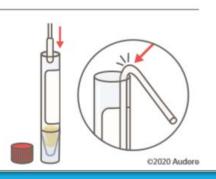


3 Put swab in tube

Lower the swab, tip first, into the provided tube.

Once the tip is at the bottom, break the swab handle at the top of the tube by bending back and forth.

Screw the red cap on tightly.



1. Instructions developed by Audere

LABCorp:

COVID19

home collection

(polyester nasal/saline)

Kit includes:



April 21, 2020

Intended use: to collect a nasal swab for purpose of in vitro diagnostic testing in a CLIA laboratory. Rx only



Distributed by Pixel by LabCorp 531 South Spring Street Burlington, NC 27215

PXC42420-4

LABCorp: COVID19 home

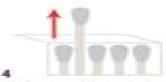
collection

Self-Collection kit instructions

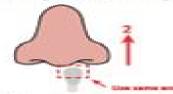
For In Vitro Diagnostic Use



When you are ready to collect your sample, register your kit online at www.pixel.labcorp.com/register and type in the 12-digit barcode located on your collection tube.



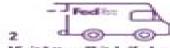
Take one of the cotton swabs out of its package. Do not touch the cotton tip of the swab with your hands. You will only need one of the cotton swabs but the rest have been provided as backups.



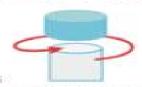
Take the cotton swab out of your nostril. Using the same end of the cotton swab, repeat step 6 in your other nostril.



Fold the other half of the gel pack on top of the specimen bag. Place the specimen bag and gel pack into the insulated foil pouch. Remove the adhesive cover strip to seal the insulated foil pouch. Gel pack and specimen bag must be included in foil pouch for lab to generate a result.



Visit https://bit.ly/fedexdropbox to view FedEx drop box locations and pickup schedules. It's important to bring your sample to a drop box on the same day you collect it before the last Express pick up. Do not deliver sample to a drop box on Saturday or Sunday. Do not take to a FedEx office. Or refer to the flyer in your kit to schedule a FedEx pickup on the day of collection.



Screw off the top of the collection tube. Hold swab in one hand and collection tube in the other being careful not to spill the liquid. Do not drink the liquid.



Remove the cotton swab from your second nostril and place in the collection tube. The end of the cotton swab that went into your nose should be placed into the tube first so that it sits down in the liquid. Screw the top of the collection tube back on.



Pface the insulated foil pouch into the shipping box and close the lid. Pface the shipping box into the FedEx return pack. Remove the adhesive cover strip and seal the FedEx return pack closed.



Wash and dry hands before opening the kit. Open your kit and place all the contents on a clean, dry surface.



Insert the tip of the cotton swab into one nostril. The cotton swab does not need to be inserted far – insert just until the cotton tip of the swab is no longer visible. Rotate the swab in a circle around the entire inside edge of your nostril at least 3 times.



Wash and dry hands thoroughly again. Insert collection tube into the biohazard specimen bag. Seal the biohazard specimen bag by closing the zip lock seal. Fold the specimen bag in half and lay the bag on one half of the gel pack.



Deliver the postage paid, pre-addressed FedEx return pack to a FedEx drop box. It's important to bring your sample to a drop box on the same day you collect it before last Express pick up. Do not deliver sample to a drop box on Saturday or Sunday. Do not take to a FedEx office. Or refer to the flyer in your kit to schedule a FedEx pickup on the day of collection.

Everlywell:

COVID19 home collection

May 15, 2020

(foam nasal/saline)

Sample Collection Instructions

Please follow all instructions closely to ensure proper precautions are taken for packaging and sending COVID-19 samples to our collection labs. Make sure you can ship the same day you collect.



Register

You must register your kit at everlywell.com/register before you collect. This lab cannot process your sample if this step is missed.



Locate drop box

Check your return label to determine if your package will be shipped via FedEx or UPS. Visit the carrier's website to view drop box locations and pick up schedules. Do not deliver sample to a drop box on the weekend. Drop off your sample on the same day you collect before the last pickup.



Fill out kit ID sticker

Place sample ID sticker on the collection tube. Write your full name, date of birth, and the date of collection. Do not pour the liquid out of the tube.



Prep for collection

Disinfect surfaces where you will be completing your test. Blow your nose. Then thoroughly wash your hands with soap and water for 20 seconds prior to collection.



Position your head

Tilt your head back to approximately a 45 degree angle.



Insert nasal swab

Gently and slowly insert the swab into your nostril, parallel to your mouth, about 2-4 cm until resistance is met. The stopper on the shaft of the swab should not go past the edge of your nostril.



Collect swab sample

Rotate the swab 3 times all the way around the nasal wall with a slight pressure. Repeat this process in the other nostril using the same swab.



Place the swab sample in the tube

Put the swab (tip down) into the tube. Hold the tube away from your face and break the swab at the perforated line. Leave the swab in the tube, and don't spill the liquid. Tightly seal cap.



Place tube into bag

Place absorbent sheet and sample tube into the protective biohazard bag. Follow return instructions on the reverse.

Everlywell: COVID19 home collection

Return Instructions

Double check that you registered your sample at <u>everlywell.com/register</u> and added the sample ID sticker with your information to the sample tube.



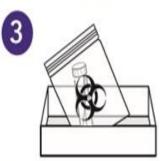
Wash your hands

Wash your hands thoroughly with soap and water for 20 seconds.



Assemble box

Assemble your shipping box.
Watch our box assembly video at everlywell.com/collect.



Prepare sample

Place your biohazard bag inside the box. The box provides extra protection during transit.



Put box in mailer

With clean hands, place the shipping box into the prepaid mailer. Apply the shipping label to the front of the envelope.



Alcohol prep pad



Disinfect the mailer

Use the provided alcohol prep pad to disinfect the mailer, avoiding the address label, before completing the final shipping step.



Ship

Deliver the pre-paid, pre-addressed return pack to the appropriate carrier's drop box. It's important you drop off your sample on the same day you collect before the last pickup for overnight shipping. Do not deliver sample to a drop box on the weekend.

SARS-CoV-2 ASSAY (Rutgers Clinical Genomics Laboratory)

May 7, 2020



Patient Self-Collection Kit and Collection Process SOP - Telehealth

Test package dispatched and sent via express carrier or USPS including:



Instruction card



Spectrum SDNA-1000 Saliva Collection Device



Lab-Loc Specimen Bag for Biohazard



Alcohol Prep Pad

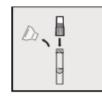


Overnight carrier overpack UN 3373 Biological Substance Category B





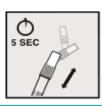
Step 2

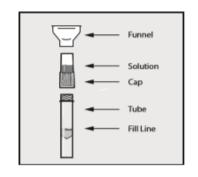


Step 3



Step 4





Do NOT eat, drink, smoke, or chew gum for 30 minutes before giving your saliva sample.

Fill the tube with saliva to the black wavy line.

Fill the tube until your saliva (not including bubbles) is at or just above the wavy line. <u>DO NOT OVERFILL</u>.

Replace the funnel with the fluid cap.

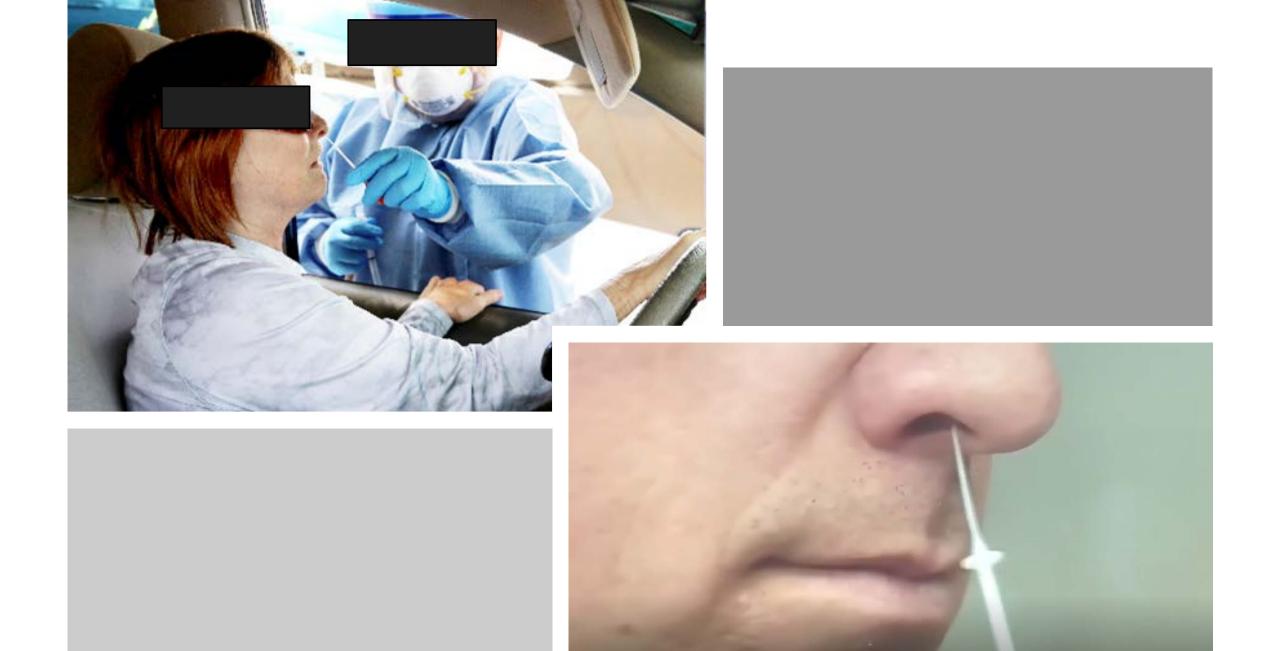
Remove the funnel from the tube. Screw on the enclosed cap <u>TIGHTLY</u> to release the solution that will stabilize the DNA in your saliva.

Firmly screw cap down to release solution and seal tube.

You will know it works when the blue solution from the cap is released into the tube. Firmly tighten cap to assure the cap and tube is completely sealed.

Shake the tube for at least five seconds.

This will ensure your sample mixes thoroughly with the <u>stabilizing</u> solution.



SARS-CoV-2 Specimen Collection

Collect an adequate specimen

- From the correct site
- Use appropriate sampling device/media/ transport

Collection and transport devices are <u>essential</u> components of the preanalytical process of microbiology testing.

These early steps in the preanalytical process are <u>critical</u> to production of clinically relevant information.





https://www.fda.gov/medical-devices/emergency-situations-medical-devices/faqs-testing-sars-cov-2#whatif

