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Alameda County COVID-19 Laboratory Testing Guidance for Clinicians—July 2020

This guidance is intended to assist clinicians and health care facilities to use the most appropriate laboratory tests to identify current infection with SARS-CoV-2, the virus that causes COVID-19.

Available Test Types

Nucleic Acid Amplification Tests (NAATs)

The preferred and most common laboratory test for diagnosing active COVID-19 infections is a nucleic acid amplification test (NAAT). There are several types of NAAT tests approved by the FDA Emergency Use Authorization (EUA) for COVID-19 testing – e.g., a real time Reverse Transcription Polymerase Chain Reaction (RT-PCR) test, which is utilized by the CDC and UCSF Covid-19 assay; Transcription Mediated Amplification (TMA), utilized by the Hologic Panther system, etc. These are all molecular testing platforms that detect viral nucleic acids.

NAAT tests, run in laboratories that are designated by CLIA as "moderate or high complexity", whether they are RT-PCR or TMA-based tests, are preferred for identifying active infection in both symptomatic and asymptomatic patients. Sensitivity and specificity are comparable among many of the testing platforms run in a moderate/high complexity CLIA laboratories. While specificity among commercial tests are high, sensitivity may vary depending on a number of factors, including the anatomic site and timing of collection during the course of infection.[i] NAAT tests that are run in a CLIA-waived laboratory may have different sensitivity/specificity as compared to assays run in a CLIA moderate/high complexity laboratory. Thus, it will be important to fully assess the test prior to bringing it online in your facility. The two point-of-care assays that can be run in a CLIA-waived laboratory such as a physician's office are the following:

- **Abbott ID NOW** is an isothermal NAAT. This is a CLIA-waived, point-of-care test (results available within 15 minutes) which is highly specific but considerably less sensitive in comparison to RT-PCR. As of June 19, 2020, an increasing number of reports have been filed with the FDA regarding false negative results as compared with other molecular assays. For this reason, negative results are considered "Presumptive Negative" and additional reports[ii] have shown that there may be the potential for false positive results if adequate cleaning of the instrument is not performed. Thus, re-testing of patients on another molecular testing platform is recommended for "presumptive negatives" as well as positive samples from asymptomatic persons without known exposures.

- **Cepheid GeneXpert® Xpress SARS-CoV-2** is a CLIA-waived, rapid point-of-care test using RT-PCR (results available within an hour). The sensitivity and specificity of this test are comparable with other RT-PCR assays offered in moderate/high complexity CLIA laboratories. Negative samples are considered negative.

Antigen tests

Two rapid SARS CoV-2 antigen tests are now available for point-of-care use, under FDA Emergency Use Authorizations (EUAs). Both tests qualitatively detect nucleocapsid protein from SARS-CoV-2. Although these tests are highly specific, their sensitivity is significantly lower than most molecular (NAAT) assays. Negative test results using antigen tests should be considered presumptive and should be confirmed using a non-point-of-care NAAT. For this reason, rapid antigen tests are generally recommended for use when pre-test probability is high – i.e., in symptomatic patients during the first 5 days of illness, in populations with a high prevalence of disease. The primary advantages of these tests are their portability and rapid turnaround time. Positive results may expedite clinical and infection control decisions.

According to the Association of Public Health Laboratories (APHL) rapid SARS-CoV-2 antigen tests should generally NOT be used for screening asymptomatic individuals, including healthcare workers and emergency responders, and should not be the primary tests considered when expanding testing to underserved populations.

- The **BD (Becton Dickinson) Veritor System for Rapid Detection of SARS-CoV-2** should be run on nasal swabs ONLY and has a turnaround time of 15 minutes. Clinical studies run by the manufacturer documented 84% sensitivity and 100% specificity using this assay. The FDA EUA states that this test is indicated in "individuals who are suspected of COVID-19 by their healthcare provider within the first five days of the onset of symptoms."
- The **Quidel Sofia 2 SARS Antigen FIA** may be run on NP or nasal swabs and has a turnaround time of 15-30 minutes. Its sensitivity is estimated at 80%, with a specificity of 100%. The FDA EUA for this assay also states that the test is indicated for "individuals who are suspected of COVID19 by their healthcare provider within the first five days of the onset of symptoms." The Quidel Sofia 2 SARS Antigen FIA assay does not differentiate between SARS-CoV and SARS-CoV-2.

Serological testing

Serological testing (i.e. antibody testing) for surveillance and research purposes is beyond the scope of this guidance. Serological testing for diagnosis of acute COVID-19 infection is not currently recommended. Refer to the ACPHD Serological Testing for COVID-19 FAQ for more information on serological testing. Serological testing is recommended to support a diagnosis of Multisystem Inflammatory Syndrome in Children (MIS-C); see the ACPHD Health Alert for more information.

Guide to collecting specimens from the respiratory tract to detect SARS-CoV-2

The table below is designed to assist clinicians to understand and evaluate the different types of specimens that may be used to diagnose SARS-CoV-2 infection in patients.

For initial diagnostic testing for the presence of SARS-CoV-2, Alameda County recommends collecting and testing an upper respiratory specimen. If the initial upper respiratory sample result is negative and the suspicion remains high, a lower respiratory tract sample may be appropriate – for example, in patients who are intubated or who have a tracheostomy. Sputum induction to diagnose SARS-CoV-2 is NOT recommended, as this is an aerosol-generating procedure that may pose unnecessary risk to healthcare workers. In situations where patients have developed a productive cough, especially if they are hospitalized, clinicians should consider collecting and testing sputum from the lower-respiratory tract.

There are several options for collecting a swab from the **upper respiratory tract** that could be performed either **by health care personnel or supervised onsite self-collection**. Studies in the past have found NP swabs to be more sensitive than OP swabs for detecting other human coronaviruses, and a combination of NP and OP swabs to be more sensitive than either alone[iii]. However, current studies find that anterior nasal or nasal mid-turbinate specimens, even self-collected with supervision, may yield specimens which have sensitivities comparable to NP swabs.[iv] [v] When possible, for increased sensitivity, consider collecting swabs from two anatomical sites. Salivary specimens are not currently recommended but their utility is under study and initial research appears promising.[vi]

Respiratory specimen collection to detect SARS-CoV-2			
Tract	**Anatomic Site**	**Collection**	**Comments**
Upper Respiratory Tract	Nasopharyngeal (NP) swab	Use only synthetic fiber swabs with plastic or wire shafts. Do not use calcium alginate swabs or swabs with wooden shafts, as they may contain substances that inactivate some viruses and inhibit PCR testing.	The NP swab is collected by a health care provider from the posterior nasal pharynx, making this collection method the most likely to result in the patient sneezing or coughing, thus generating potentially infectious aerosols.
	Oropharyngeal (OP) swab		For increased sensitivity, consider collecting a swab from a second anatomical site.
	Nasopharyngeal wash/aspirate or nasal wash/aspirate (NW)	Attach catheter to suction apparatus.	Specimen and the non-bacteriostatic saline used to collect the specimen should be placed immediately into a sterile transport tube.
	Nasal mid-turbinate swab	Use a flocked tapered swab.	May be collected by patient when supervised by a health care worker.
	Anterior nares (nasal swab)	Use a flocked or spun polyester swab, sample both nostrils with same swab.	
Lower Respiratory Tract	Bronchoalveolar lavage	Collect 2-3 mL into a sterile, leak-proof, screw-cap sputum collection cup or sterile dry container.	Most often used in hospitalized patients who are receiving invasive mechanical ventilation.
	Endotracheal aspirate		
	Expectorated sputum	Expectorate deep cough sputum directly into a sterile, leak-proof, screw-cap collection cup or sterile dry container.	For patients with productive cough only. Induction of sputum is NOT recommended.
		container.	

Specimen Collection

The CDC has provided guidelines for collecting, handling, and testing clinical specimens for COVID19, which include PPE requirements, techniques to prevent contamination of swabs, and techniques for specimen collection.

- **Specimen Collection Instructions**

Proper collection of specimens is the most important step in the laboratory diagnosis of infectious diseases. A specimen that is not collected correctly may lead to false negative test results. For more

information, including illustrations and step-by-step guidance applicable to respiratory viruses in general, see the CDC Influenza Specimen Collection instructions. The New England Journal of Medicine's How to Obtain a Nasopharyngeal Swab Specimen guidance presents written visual, and video aids for collecting an NP swab.

- **Swab Type**

  Swab specimens for COVID19 testing should be collected using only swabs with a synthetic tip, such as nylon or Dacron®, and an aluminum or plastic shaft. Calcium alginate swabs are unacceptable and cotton swabs with wooden shafts are not recommended.

- **Multiple sites**

  Consider collecting samples (no more than two) from multiple upper respiratory sites to increase sensitivity. If two swabs are collected, they should be combined in a single tube to maximize test sensitivity and limit use of testing resources.

- **Transport**

  Unless otherwise indicated, all swabs should be placed immediately into a sterile transport tube containing 2-3mL of either viral transport medium (VTM), Amies transport medium, Universal Transport Medium (UTM), sterile saline, or a transport medium provided by the reference testing laboratory; unless using a test designed to analyze a specimen directly, (i.e., without placement in VTM), such as some point-of-care tests.

- **Self-collection at home**

  There are several tests for active infection that may become available in the near future for home-based collection. Testing of saliva samples using a PCR-based test is currently being evaluated by researchers. Antigen tests, which look for proteins located on the outside of the virus, could be performed at home. **No home-based collection tests are currently being recommended by Alameda County for diagnosis of active infection.**

Bay Area Laboratories

Besides using the correct specimen collection method from the most appropriate anatomic site, work with your laboratory to understand their specific processes and procedures. For example, tracheal aspirate specimens may take longer to process than NP/OP swabs at some laboratories, and not all laboratories are properly validated to test these specimens.

Use the table below to identify area laboratories that can process clinical specimens and their preferred swab type and transport media.

Testing Laboratories and Testing Kit Supplies		
Testing Lab	**Swab Type**	**Transport Media and Contact**
Alameda County PHL	Nasal/NP/OP swab Provided by AC PHL Contact: Kristina.hsieh@acgov.org	Provided by AC PHL Contact: Kristina.hsieh@acgov.org
UC Berkeley (IGI)	Nasal/OP swab Provided by UC Berkeley Contact: lwitkowsky@berkeley.edu	Provided by UC Berkeley Contact: lwitkowsky@berkeley.edu
UCSF (Chan Zuckerberg)	No swabs available Contact: Kristina.hsieh@acgov.org for supplies	Provided by UCSF, but they can accept VTM/UTM/Saline Contact: robert.puccinelli@czbiohub.org
Stanford	No swabs available Contact: Kristina.hsieh@acgov.org for supplies	Accept VTM/UTM/Saline, contact EMS for supplies. Stanford Contact: 1877-717-3733
Avellino	Provides Floq Swabs Contact: scott@avellino.com	Provided by Avellino Contact: scott@avellino.com
Quest Diagnostics	Provided by Quest Contact: 1866-697-8378 If supplies run out, Contact: Kristina.hsieh@acgov.org for supplies	Provided by Quest Contact: 1866-697-8378 If supplies run out, contact EMS
LabCorp	Provided by LabCorp https://www.labcorp.com/provider-services If supplies run out, Contact: Kristina.hsieh@acgov.org for supplies	Provided by LabCorp https://www.labcorp.com/provider-services If supplies run out, contact EMS
Kaiser	Currently not accepting testing for Non-Kaiser member. If a Kaiser member, request testing through Kaiser doctor.	
Sutter	Willing to accept non-Sutter patients for testing. Only testing symptomatic people. Call 866-961-2889 to inquire about whether your patient qualifies for testing.	

Verily	Contracts with Quest/LabCorp for Testing. Contact Verily for more questions about obtaining testing for your patients. Contact: contact@projectbaseline.com	
Additional Laboratory Testing Facilities Across California	https://testing.covid19.ca.gov/wp-content/uploads/sites/332/2020/07/COVID-19-Testing-Task-Force-Lab-List-updated-07_16_20.pdf	
California Department of Public Health sponsored free INDIVIDUAL COVID-19 Testing Sites	https://testing.covid19.ca.gov/	
Alameda County Public Health Department sponsored free COVID-19 Testing Sites	http://www.acphd.org/media/571443/alameda-county-covid-testing.pdf	

Resources and Links

- Alameda County Department of Public Health Testing for COVID-19 Information
- Alameda County Department of Public Health Testing Sites
- CDC Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19
- Alameda County COVID-19 Testing Supplies Survey- If your organization needs testing supplies specifically for the COVID-19 testing, please complete this survey.
- Nasal (Anterior Nasal) Specimen Collection for SARS-CoV-2 Diagnostic Testing (Nasal (Anterior Nasal) Specimen Collection for SARS-CoV-2 Diagnostic Testing Factsheet
- New England Journal of Medicine How to Obtain a Nasopharyngeal Swab Specimen

[i] Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. JAMA. 2020;323(22):2249-2251. doi:10.1001/jama.2020.8259

[ii] Pradhan R. Problems With Trump-Touted COVID-19 Test Pile Up. Kaiser Health News. https://www.thedailybeast.com/problems-with-trump-touted-abbott-rapid-covid-19-test-pile-up. Published June 19, 2020. Accessed June 19, 2020.

[iii] Lieberman D, Lieberman D, Shimoni A, Keren-Naus A, Steinberg R, Shemer-Avni Y. Identification of respiratory viruses in adults: nasopharyngeal versus oropharyngeal sampling. J Clin Microbiol. 2009;47(11):3439-3443. doi:10.1128/JCM.00886-09

[iv] Tu Y-P, Jennings R, Hart B, et al. Patient-collected tongue, nasal, and mid-turbinate swabs for SARS-CoV-2 yield equivalent sensitivity to health care worker collected nasopharyngeal swabs. medRxiv. Published online April 6, 2020:2020.04.01.20050005. doi:10.1101/2020.04.01.20050005

[v] Self-collection: an appropriate alternative during the SARS-CoV-2 pandemic - Abstract - Europe PMC. Accessed June 10, 2020. https://europepmc.org/article/ppr/ppr150237

[vi] Self-Collected Oral Fluid and Nasal Swabs Demonstrate Comparable Sensitivity to Clinician Collected Nasopharyngeal Swabs for Covid-19 Detection | medRxiv. Accessed June 10, 2020. https://www.medrxiv.org/content/10.1101/2020.04.11.20062372v1