Clinical Laboratory COVID-19 Response Call

March 30, 2020

Moderator
Jasmine Chaitram, CDC Division of Laboratory Systems

Panelists
Wendi Kuhnert-Tallman, CDC Laboratory Task Force
Tim Stenzel, U.S. Food and Drug Administration (FDA)
Karen Dyer, Centers for Medicare & Medicaid Services (CMS)
Janet Hamilton, Council for State and Territorial Epidemiologists (CSTE)
Bill Arndt, CDC Division of Laboratory Systems

JASMINE CHAITRAM: Hello again, everyone. Thank you for joining us today. My name is Jasmine Chaitram. I'm the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems at CDC.

Our division works to advance quality and safety, data and biorepository science, and workforce competency across the US clinical laboratory community. We also work closely with clinical and public health laboratories across the country to support laboratory emergency preparedness and response activities. Throughout the COVID-19 response, we've been supporting CDC's emergency operation center by serving as an interface between CDC and the clinical and public health laboratory communities. Some of the tasks that we've been focused on include laboratory biosafety, the regulatory requirements under the Clinical Laboratory Improvement Amendments Act, known as CLIA, and additional laboratory quality issues, and the challenges associated with implementing laboratory-developed tests.

On these weekly calls, we will discuss hot topics and solicit the community's questions about the work that clinical laboratories are doing to support the nation's response to COVID-19 pandemic. We hope these calls are useful to you, as we want to create a platform for CDC and other government agencies and clinical laboratories to engage with and learn from one another. We structured the content of this week's call based on the frequently asked questions that we receive as well as other inquiries that we received throughout the week. And thanks to those of you that have submitted questions during the last call.

Because we anticipate a large number of participants on this call and we expect to have a lot of questions, we may not be able to directly and immediately address every issue. However, we will note your questions and feedback and tailor the content of our future calls accordingly. As I said, we want this call to be useful and relevant to your COVID-19 response activities, so please submit those questions.

The best way to submit those questions for consideration is by using the question and answer Q&A function in Zoom or by emailing DLSinquiries@CDC.gov. For media questions, please contact CDC Media Relations at media@CDC.gov. And if you are a patient, please direct any questions to your health care provider.

WENDI KUHNERT-TALLMAN: Some topics I touched upon last week and will provide a little bit more information on. The first is serology testing.

The CDC has developed and optimized a set of serological assays to detect SARS-CoV-2 antibodies in serum. These assays use the SARS-CoV-2 spike antigen designed and produced by the Vaccine Research Center at NIH as well as the live virus that CDC isolated in February. These assays specifically detect antibodies against SARS-CoV-2 and not antibodies against common coronaviruses that have already infected many individuals.

Related to distribution, we have used these assays in several contact investigations to monitor immune responses. We are also preparing to deploy them to larger sero surveys within the coming weeks to further identify individuals who, due to mild infection, may not have known they were infected with SARS-CoV-2, and also to monitor immunity in recovered individuals. CDC does not intend to pursue an EUA for this assay at this time due to the fact that we don't intend to use this for diagnostic purposes. Work is ongoing within the overall US government effort to determine next steps for potential evaluation of existing serologic assays as well as others that may be submitted for an EUA.

So one of the other things I was asked to talk about was updated guidance on specimen collection and transport for COVID-19 testing. On March 25, CDC posted updated guidance on specimen collection and transport for COVID-19 testing. CDC labs have been researching ways to make COVID-19 testing easier to conduct, and have been in contact with other laboratories doing the same, as well as in coordination with FDA. This guidance takes advantage of these laboratory findings to allow more flexibility in obtaining specimens for COVID-19 diagnosis.

Specifically, when collecting a nasopharyngeal swab, or when collecting a nasopharyngeal swab is not possible, the new guidance allows for a nasal swab specimen to be used instead. The nasal swab specimen is easier to collect, and less unpleasant for the patient, and does not require that the health care provider wear extensive PPE that is needed when an NP swab is being collected. This new guidance also allows for people to collect their own nasal swabs when under supervision by a health care provider, which again, further reduces the burden on health care staffing requirements. A question that might come up related to this is, has CDC verified that this method is effective? On March 23, FDA approved the use of nasal swabs for collection of SARS-CoV-2. FDA guidance now allows for a specimen to be sent in sterile saline when the recommended viral transport medium is unavailable. And currently, I think most are aware that VTM is in short supply.

The self-administered nasal swab was recently determined to be equivalent to a nasopharyngeal swab in detecting coronavirus through a study performed by the UnitedHealth Group. As a result of these data, the FDA recommended a self-collected nasal swab and self-collected mid-turbinate swabs for use in addition to NP swabs, and this information is available on the FDA frequently asked questions site. So following that, research has also shown, I think as evident, that the nasal swab is less invasive, results in less patient discomfort, and there is evidence of comparable accuracy among nasal and nasopharyngeal specimens collected for the purposes of viral diagnostics.

Another thing that we were asked to speak on today was the fact that CDC has released updated guidance on evaluating and testing persons for coronavirus disease. Limited information is available to characterize the spectrum of clinical illness associated with COVID-19. And please be reminded that no vaccine or specific treatment is available at this time and that care and treatment is generally

supportive. So CDC has developed clinical criteria for considering testing of COVID-19 and has published this on our website.

We consider there to be a number of categories. Priority one testing would include hospitalized patients, health care facility workers, with symptoms. Priority two would then include patients in long-term care facilities with symptoms, patients over 65 years with symptoms, patients with underlying conditions with symptoms, and first responders, again, with symptoms. Priority three would then include critical infrastructure workers, again, with symptoms, individuals who do not meet any of the above categories with symptoms, health care workers, and first responders, an individual with mild symptoms in communities experiencing high numbers of COVID-19 hospitalizations.

CDC maintains several dissemination channels to share real-time updates with health care providers across the country. We want to ensure that every clinician that is on the front lines has the information that they need to do their jobs effectively. And CDC has a number of methods of distribution, and please note that we are working with our Medical Countermeasures Task Force to ensure that this updated guidance is shared more widely. Thank you.

JASMINE CHAITRAM: Is there any plan from CDC to provide supplies to laboratories that perform COVID-19 testing, such as RNA extraction kits or swabs?

WENDI KUHNERT-TALLMAN: At this time, CDC does not have plans to change our process of distributing reagents through the IRR to state and local public health labs. CDC has not distributed swabs or VTM in the past, and at this time, we don't anticipate that to change. We understand that all of these items are in short supply, and CDC is reviewing data from other platforms, as well as other collection methods, that will hopefully limit the need for some of these reagents that are in short supply. But at this time, our research is not yet final, and so we're not able to share final results.

JASMINE CHAITRAM: Throat swabs have been shown in several studies so far to have a sensitivity of only about 30%. Is the CDC still saying that this is an acceptable swab in the absence of an NP swab?

WENDI KUHNERT-TALLMAN: So CDC has looked at this. And in our review, there is some loss of sensitivity with an OP swab alone. The loss is not as significant as was stated in that paper. I believe the loss that we saw was less than 40%, recognizing that is still a significant number.

But our concern is that, in many circumstances, this may be the only swab that's available. And we feel like testing, especially in these priority categories, is warranted. We also feel that in a symptomatic person who meets the criteria for testing, generally speaking, the viral load has been found to be significant enough that it should not be impacted as significantly by the swab type.

JASMINE CHAITRAM: Can a rapid serological test made abroad for COVID-19 be distributed at point of care testing without verification in the US labs?

TIM STENZEL: I'm not sure what's meant by verification. Labs that are using it would want to test positive and negative controls before putting it into service. But this would be a CMS or CLIA mandate, not necessarily an FDA mandate.

JASMINE CHAITRAM: They may have meant validation. Or are there any other regulations that need to be followed for a test that's made abroad being used in the US?

TIM STENZEL: So for claims that have to do with detection of IgG and IgM, the manufacturers that are listed on the FDA website under the FAQs are not required to be validated in the labs that are going to use them in the United States.

JASMINE CHAITRAM: If point of care testing is positive, does the test need to be confirmed by a diagnostic molecular test?

TIM STENZEL: I'm going to assume that it's a molecular point of care test, in which case I would refer to the package insert or instructions for use with the EUA authorized device. In general, though, no.

JASMINE CHAITRAM: Can non - diagnostic instruments or RUO instruments be used, as long as there's appropriate documentation?

TIM STENZEL: So absolutely, non-diagnostic instruments can be used. If the lab is using an EUA authorized kit-- this is for CLIA labs-- they can do a bridging study.

As long as it passes their validation, they can begin testing using the alternate instrument, and there is no requirement for an FDA EUA submission or amendment. If the lab is using it to develop their own LDT, then if they're in a state that will do the review for the FDA or in lieu of the FDA's, then they can go through their state. If their state has not requested that authority, then they can come into the FDA by notifying us that they've validated their assay, and following up with an EUA submission within 15 different business days.

We're continuing to work hard to authorize additional EUA kits. We are reviewing some serology assays for EUA authorization. We hope to do that this week. We continue to invite all test developers, including CLIA labs, to develop tests. And if we can help in any way, please reach out to us.

KAREN DYER: We issued a memo March 26 to provide guidance during the public health emergency for COVID.

A lot of the information in here is in response to questions that we have received. I'm going to go through and hit the high points of the memo. But just be reassured that we are committed to taking steps to ensure that labs are prepared to respond to COVID-19, and to assure reliable testing, as well as patient health and safety.

The memorandum, the information in that, and the guidance, is only applicable during the public health emergency for COVID-19. And if you have labs that are accredited, they need to follow their accrediting organization requirements. They also need to be aware of state laws, if they are more stringent than the CLIA requirements.

So during this state of emergency and in responding to things, we are generally focusing our efforts on addressing situations that rise to the level of immediate jeopardy and exercising enforcement discretion for activities that do not rise to that level. So I'll move on to talk about remote review of lab data results in slides. This has probably been the biggest area we've gotten comments on. And as we've done in

previous emergencies, we're going to exercise enforcement discretion here. And we will not enforce the requirement to have a separate certificate for labs that are located at temporary testing sites, provided that that designated primary site or home base has such a certificate using the address of the primary site and the work being performed in the temporary testing site falls within the parameters of the primary site certificate.

We have criteria that we've listed on the memo, that if you are a lab that wants to utilize the temporary testing site option, that you will need to meet in order to do that. I'm not going to go into all of them. There's like five of them on the memo. It's important to note that this guidance does not apply to pathologists who already have obtained CLIA certificates for their home or other sites separate from the primary testing site.

We've gotten a lot of requests for expedited CLIA applications for laboratories to get labs up and running as quickly as we possibly can. To ensure that the labs are going to be able to do this, we've reviewed the regs. And we have gone through a procedure that says, once the laboratory has identified a qualified laboratory director and provided all required information on the 116 application, it will be processed, and the state will assign a CLIA number to that laboratory. We are going to allow for testing, once the CLIA number has been assigned, as opposed to waiting for the hard copy paper certificate to come in the mail. Once the CLIA number has been assigned, as long as the laboratory has done and followed the applicable CLIA requirements, such as establishing performance specs, they can begin testing.

We've gotten additional questions about proficiency testing. Please note, that only CMS can allow postponement, suspension, or cancellation of CLIA-required PT activities while patient testing continues. If a PT provider can't provide the testing or is having issues, they need to notify CMS accrediting organizations, exempt states, and their laboratories. Should CMS determine that PT should be postponed, suspended, or canceled, CMS will authorize the PT programs to use reason code 10.

Labs will also need to make sure that, if they do not perform PT as a result of these, that they make sure they keep all the documentation with what they receive from the PT provider as well. If the lab temporarily suspends performing a specific lab test due to staffing shortages, supply issues, reagent shortage, the lab must document the time frame during which the test is not being performed and the reason why. And they must notify their inspection agency and the PT program within the time frame of submitting their PT results that the lab has stopped testing and the reason for them to stop testing.

We had an earlier speaker that talked a little bit about the specimen collection, and the swabs, and so forth. CLIA regulations are not prescriptive about the type of transport device, for example, specimen collection swabs and viral transport media, that the laboratories are currently using. We require the laboratory follow the manufacturer's instructions. And obviously, if a lab modifies the manufacturer's instructions, the lab must establish performance specs and validate the assay prior to patient testing. We are not prescriptive on that aspect.

During a public health emergency, according to FDA, when one entity establishes equivalent performance between parallel testing of the same specimens with the new and original components-- excuse me-- including viral transport media and FDA's review of the validation data, it indicates that it could be applicable to modifications of other tests with an authorized EUA. And the laboratory involved agrees to FDA to share that information for use by other labs. FDA has posted this information on its website so other labs can refer to the validation for their testing without conducting their own bridging

study for the same modification. In instances where the FDA has indicated that certain alternative collection devices and specimen transport media can be used, the CLIA laboratory director will need to decide if subsequent validation studies are needed before the tests are performed.

And I just want to touch base on the laboratory-developed test issue. FDA published guidance on March 16 entitled, "State Authorization of Labs Certified Under CLIA," that meet the CLIA regulatory requirements to perform high-complexity testing. This guidance explained that states may take responsibility for tests developed and used by the laboratories in their states, similar to the action the FDA granted to the New York State Department of Health.

States can choose to set up a system in which they take responsibility for authorizing such tests, and the laboratories will not engage with the FDA. The guidance goes on to say that the FDA requests that the state or territory notify FDA if they choose to use this flexibility to expedite COVID-19 testing. If your state has not chosen to validate laboratory-developed tests, you need to refer to the FDA for further guidance.

States that cannot stand up their own oversight systems may choose to continue having laboratories submit test validations and notifications of patient testing to the FDA. We still want to clarify that labs performing LDTs as set forth in the FDA guidance are required to be CLIA certified and meet the requirements to perform high-complexity testing.

JASMINE CHAITRAM: With the shortage of supplies and in the absence of individual quality control plans with EUA testing, do labs still have to run positive and negative controls daily as required by CLIA?

KAREN DYER: Well, the manufacturer's instructions for all tests that have an authorization for use as an EUA must be followed, to include quality control. If the FDA has granted an EUA authorization for a specific test, the laboratory must follow the approved verification process outlined in the manufacturer's instructions.

JASMINE CHAITRAM: Originally, CMS did not approve pathologists working remotely during this public health emergency. Has that changed?

KAREN DYER: CMS will allow laboratories to utilize temporary testing sites for remote review and reporting of laboratory data, slides, images, as long as the criteria that we spelled out in the memo are met. Obviously, I'm going to refer back to our memo, QSO-20-21-CLIA, "Lab Guidance During the COVID-19 Public Health Emergency."

JANET HAMILTON: Thank you all for your time and tireless work collecting laboratory data. My name is Janet Hamilton. I am with the Council of State and Territorial Epidemiologists, and I represent those epidemiologists primarily in state and local health departments that are the disease detectives working this outbreak and conducting case investigations to determine when and where cases are occurring, and to implement control measures, as well as to evaluate those control measures. The laboratory data that you all are producing is one of the most vital pieces for those epidemiologists to identify those cases and to begin to investigate those case investigations.

I wanted to highlight a couple of things for you all as laboratories. The first is that it is critical to report identifiable data rapidly to the state health department. It is that identifiable data that allows them to

initiate those case investigations, and summarize case counts effectively, as well as pass that information along to CDC, who we work very closely with. Additionally, submitting that data to state and local health departments fulfills your regulation as a laboratory, meeting state mandates or state law to report data for diseases of public health significance to the health department.

I also want to just fully recognize, that as laboratories, you all are getting a lot of requests from different levels of government to report this critical data. And I want to really emphasize that it is the data that goes to state and local health departments that allows that initial front line response. And so thank you so much for prioritizing that information so that those case investigations can occur.

I wanted to highlight a challenge that we are seeing for those laboratories that are submitting data. And that is, we are seeing an increasing number of results getting submitted with missing patient information, in particular, patient address information. The patient's residential address, including if they're in a nursing home, is really critical to being able to pinpoint hot spots. So again, just working with your submitters to really improve that critical information is vital to this response.

And also, as you are coming online with new testing, please reach out to your state health departments so that you can initiate the disease reporting pieces of that identifiable information rapidly. States also require this to be submitted in electronic formats. And again, thank you so much for your tireless work.

BILL ARNDT: I would like to provide you an update on the revised COVID-19 laboratory biosafety guidance. The guidance was recently updated to recommend isolates and cultures of SARS-CoV-2 can also be shipped as Category B infectious substances. At this point then, the CDC is recommending that all COVID-19 patient samples and SARS-CoV-2 isolates or cultures be packed and shipped as Category B infectious substances.

Additionally, I would also like to highlight a couple of other topics and issues the CDC is in the process of developing guidance to address, and some of these are based on questions we received previously. The first, the CDC is in the process of developing additional guidance for decontamination and reuse of PPE. We received a number of questions on this topic last week, and we are working on developing guidance to address this PPE shortage by providing potential solutions for the decontamination and reuse of PPE.

Secondly, we are also in the process of developing biosafety guidance related to the use of certain cell lines being used in respiratory viral culture panels to detect other respiratory diseases, such as influenza, pair influenza, RSV, and others. The CDC recently sent out a LOCS message to recommend laboratories stop using the arm mix cell lines for respiratory viral culture panels. Based on current information available related to the growth of the original SARS virus and the new SARS-CoV-2 in several different cell lines, the CDC recommended laboratories stop using the arm mixed cell lines, since they are a combination of A549 and the MV1LU cells. The MV1LU cells have been shown in the past to support a low-level of SARS-CoV growth, while the A549 cells were not shown to support growth of SARS-CoV, the original SARS.

At this time, it should be assumed that the growth of SARS-CoV-2 would be similar to that of the original SARS. Until more information becomes available on SARS-CoV-2 growth in the arm mixed cell line, the CDC recommends laboratories switch to an alternate cell line that does not support growth of SARS-CoV and SARS-CoV-2. However, laboratories will have to validate their assays or panels with the new cell

lines to verify the cells will still support the growth of the viruses they are trying to detect. Now I'll turn it back over to Jasmine.

JASMINE CHAITRAM: How should phlebotomists be protecting themselves?

BILL ARNDT: So if phlebotomists or other laboratory personnel have direct contact with suspected or confirmed COVID-19 patients, they should follow the recommended PPE for health care providers while in the presence of those patients. These recommendations can be found in the CDC's interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 in health care settings, which is on the CDC's COVID-19 website under Health Care Professionals and then under Infection Control.

JASMINE CHAITRAM: Some laboratories have run out of commercial sanitizing agents and are defaulting to a bleach solution. What concentration of bleach is sufficient to kill SARS-CoV-2?

BILL ARNDT: So the guidance for the use of that concentration would be based on the initial concentration of the starting bleach concentration. So it is our recommendation to refer to the EPA's website for those chemicals and the appropriate concentration for the disinfectant at this time.

JASMINE CHAITRAM: Are there concerns around high throughput extraction methods that are on the bench, such as the Thermo Kingfisher, if these instruments cannot fit into a biosafety cabinet?

BILL ARNDT: So obviously, as we know, not all equipment can fit inside a BSC. As such, the CDC provided guidance for procedures with the high likelihood to generate aerosols or droplets. That recommendation is to use either a certified BSC, if the equipment fits. However, as we know, not all equipment will fit inside.

So additional precautions can be taken to provide a barrier between the specimen and the personnel. Our recommendation is-- examples of these additional precautions include personal protective equipment or PPE, such as surgical masks, or face shields, or other physical barriers, like a splash shield. And then the use of centrifuge safety cups, sealed rotors, to reduce the risk of exposure to laboratory personnel.

JASMINE CHAITRAM: On Friday, March 27, the CARES Act was passed and signed into law by President Trump. The CARES Act stands for the Coronavirus Aid Relief and Economy Security Act. This act explicitly states, "Every laboratory that performs or analyzes a test that is intended to detect SARS-CoV-2 or to diagnose a possible case of COVID-19 shall report the results from each such test to the Secretary of the Department of Health and Human Services in such form or manner and as at such timing and frequency as the Secretary may prescribe until the end of the Secretary's public health emergency declaration with respect to COVID-19 or any extension of such declaration." So this is about reporting to the Department of Health and Human Services.

DHHS is working with its agencies to draw out a plan for how this reporting would happen, and we hope to provide an update for that on next week's call. That would be Monday, April 6. That concludes our call for today.

These calls are occurring every Monday at 3:00 PM Eastern Daylight Time. And we encourage you to share this information about these calls with others in your laboratory and other colleagues.

We want these calls to be beneficial to you all. So please submit your questions to DLS Inquiries. We also encourage you to sign up for our messages through the LOCS communication. That's the Laboratory Outreach and Communication System, LOCS@CDC.gov.That's how we've been distributing some key messages about the response, and a lot of the guidance and a lot of the updates you heard today did go out as previous LOCS messages.

I want to thank all of our speakers for joining us and to all of you. I know everybody's busy. Thank you for joining us and taking the time to be with us this afternoon.