Clinical Laboratory COVID-19 Response Call

September 28, 2020

Agenda

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JASMINE CHAITRAM: Hi, everyone. This is Jasmine Chaitram with CDC. Thank you for joining the Clinical Laboratory COVID-19 Response Call. These calls are hosted by the Division of Laboratory Systems at CDC. This is our 20th call, so pretty excited about that. I am Jasmine Chaitram. I'm the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems.

Previous to COVID-19, we were, as a division, supporting clinical laboratories across the nation by helping with issues around quality and safety, biorepository science, data science, informatics, workforce competency and training. And we were also working on issues around preparedness and response.

And we continue to support clinical and public health laboratories on preparedness and response through the COVID-19 pandemic. And we also serve as a liaison between the CDC emergency operations center and clinical and public health laboratories.

Before we get started today, I will go through a few housekeeping things. Right now, I'm showing the agenda for today's call. We have some really good topics to discuss. First thing I want to cover, as far as housekeeping, is our next call will be on Monday, October 19.

I have mentioned before that our calls would be occurring every other week going forward. And when we looked at the schedule, the next call was going to end up on a holiday. So unfortunately, we will not have another call for about three weeks. But we will see you on Monday, October 19.

Next step is the call for any request or needs around training and workforce development. Please send those to LabTrainingNeeds@cdc.gov. We do appreciate the feedback on the training needs. As I've shown before, we have resources for laboratories within our slides. These links are here for you for easy access. And we do post the slides after the call. So you can find them on our Preparedness Portal.

There are a few slides with links for resources, as well as new information that's been posted. And we plan to continue to provide this information. We also provide some links for some of our speakers from CMS and FDA. So look in those parts of those slides for easy access to information, as well.

And we wanted to also mention that we have new codes posted for the SARS-CoV-2 antigen tests. These are LOINC codes. We have a LIVD tool, LOINC IVD tool posted on the Division of Laboratory Systems website. This is to help laboratories to easily obtain LOINC codes. We do want laboratories to use the same LOINC codes as much as possible so that we can have harmonization around these codes. It makes it easier when we're interpreting data and integrating data.

As I mentioned, the slides for this call are on the Preparedness Portal as I had mentioned on the last call. Division of Laboratory Systems recently posted or updated our preparedness portal, and now all the information for preparedness and response activities can be found in one place, including the activities that we're supporting for the COVID-19 response.

And as I mentioned, the CLCR calls-- this is what we call them, our Clinical Laboratory COVID-19 Response (CLCR) Calls-- the transcripts and the slides and the audio is also available through this portal, as well as archives of our LOCS (Laboratory Outreach Communication System) messages. Those are the emails that we send out with important information, as well. And if you're not receiving LOCS message from CDC, and you want to, please send an email to LOCS@cdc.gov, and we will add you to our distribution list.

Final housekeeping thing that I want to cover is how to ask a question during the webinar. We do have a Q&A button at the bottom of the Zoom call here. And if you would please type your question into the Q&A box and then submit it. As I've mentioned before, please include your name and email address, so that if we are not able to answer your question during this call, that we can respond to you after the call, usually by email.

Another thing with these questions is that we do use this information to help us determine topics for future agenda items. So we do appreciate all of the questions that are submitted. Apologies in advance if your question is not answered live. We do our best to get to it. But there are a lot of people on these calls and a lot of questions coming through.

So please do not be offended if we don't get to your question. As I said, we will try to either answer it by email or put it as a future topic on another agenda item on a future agenda. And if you're the media, these calls are really intended for the clinical laboratory community, as well

as public health labs, so please send your questions to media@cdc.gov, and if you're a patient, please direct your questions to your healthcare provider.

And with that we are going to go to our first speaker today, Jim Nichols. He's with the Clinical Laboratory Standards Institute, and he's going to talk about point-of-care testing resources that they have available-- Jim.

JIM NICHOLS: Thank you for the introduction, I'm Jim Nichols. I'm a medical director of clinical chemistry in point-of-care testing and a professor of pathology, microbiology, and immunology here at Vanderbilt University School of Medicine in Nashville.

I'm going to be speaking on behalf of the Clinical and Laboratory Standards Institute today on some resources that are available for those of you who are doing COVID-19 testing. Can I have the next slide?

So CLSI's focus is on the global medical laboratory community, including labs, manufacturers, and regulators. We develop, promote, and educate based on our consensus standards for laboratory testing. The membership includes more than 1,400 organizations and 400 individuals from 75 countries, based on our motto, "Fostering excellence in laboratory medicine." COVID-19 lab testing is right in our wheelhouse.

Next slide-- CLSI has identified 30 of its documents and standards that relate to COVID-19 testing, five of which are available for free. These documents cover several areas of the laboratory, including method evaluation, medical diagnostics, microbiology, general lab practices, quality management, and point-of-care testing.

So to see the list of documents, go to CLSI's home page. That's at https://clsi.org. And at the top of the page, you'll see a green bar. If you select Click Here, it will take you to a page listing the documents and other resources available. You can download a PDF of the list. You can click on one of the topic areas to see documents just on that topic. And clicking on additional COVID-19 resources will take you to information including links to government and other resources available to you.

Next slide-- now CLSI has e-learning resources, as well. And so from CLSI's home page you can click on eLearning to access free webinars for each of the COVID-19-related documents. These webinars present overviews of the contents of the documents, so that you can decide which are helpful for you.

Next slide-- there are point-of-care testing resources. Specifically, CLSI has several documents for point-of-care laboratories that are performing COVID-19 testing. POCT4 is the essential tools for implementation and management of a point-of-care testing program. This helps laboratories ensure reliable results that are comparable to those obtained from medical laboratory instruments.

We also have POCT7. That's quality-management approaches to reducing errors at the point of care. That's available for free, which helps with laboratory implementation of standard error-tracking systems with the primary goals of reducing risk, increasing quality, while accumulating standardized data for benchmark use in the future.

Next slide-- there is POCT15. This is point-of-care testing for infectious diseases, which summarizes the current knowledge of rapid and point-of-care testing practices and methods for infectious diseases.

And for nonlaboratory locations that are testing for COVID-19, such as nursing homes, prisons, pharmacies, CLSI POCT8. This is quality practices and noninstrumented point-of-care testing and instructional manual and resource for health-care workers. This document includes laboratory-science concepts and activities with the goal of increasing knowledge and quality of laboratory testing by personnel who do not have a laboratory background.

Next slide-- I'd like to thank you for your attention. Again, my email address is here. Please feel free to ask questions or to contact me after this webinar. Thank you.

JASMINE CHAITRAM: Jim, thank you so much. We didn't have any questions for you, but do appreciate CLSI sharing this information with our audience today. And I hope those of you that are using point-of-care tests will take advantage of these great resources from CLSI.

We are going to move to our next speaker, which is going to be Amy Zale from the Centers for Medicare and Medicaid Services, CMS, and Amy is going to be talking about testing and reporting requirements. This is the third call in a row that CMS has been on to answer questions related to reporting requirements and the CMS enforcement of those requirements. And we are very grateful to CMS for doing this - three calls in a row. Amy?

AMY ZALE: Thank you for having us, Jasmine. And much like the last time that we were on the call, there were questions that were asked in the chat box that we were unable to respond to live, so we've taken those questions and gotten our responses together for them. And I'm going to share them with you now.

So the first question that we were unable to answer was, Serology testing does not detect SARS-CoV2. It only tests for antibodies. Serology testing also shouldn't be used to diagnose COVID-19. How does serology testing fit the definition as stated in the regulation? The verbiage and definitions don't seem to make sense."

And regulations at 493.41 and 1100a state that, "Each laboratory that performs a test that's intended to detect SARS-CoV2 or diagnose a possible case of COVID-19 must report SARS-CoV2 test results to the secretary in such a form and manner, and at such timing and frequency, as the secretary may prescribe. Serology testing is considered testing that detects SARS-CoV2.

The next question asked, "If our LIS, Laboratory Information System is interfaced with the state, and automatically reports to the state, what type of documentation do we need? The military must have documented evidence that SARS-CoV2 test results were reported.

Surveyors will ask for and review the laboratory's policy and procedure related to SARS-CoV2 test reporting. Please note that the laboratory may have a specific policy and procedure related to SARS-CoV2 test reporting, or it may be embedded in a more general policy or procedure. Either is acceptable. Surveyors will also review SARS-CoV2 testing records. A sampling of testing records may be selected if deemed appropriate by the surveyor. Surveyors will review and verify the laboratory's documentation that SARS-CoV-2 test results were reported to state or local health department in which the laboratory is located, as well as instructions in the laboratory's policy and procedure. Please note that the laboratory must have documentation that they made an attempt to report all the SARS-CoV-2 test results performed in their laboratory.

The next question asked, "If a negative test is not reported, but used as a reflex to send to a confirmatory test, should it still be called or reported?"

The new regulations require all CLIA-certified laboratories performing SARS-CoV-2 testing to report all SARS-CoV-2 test results, including positive and negative results, to state or local health departments, as required by state and local law or policy. On June 4, 2020, the secretary of HHS published guidance related to SARS-CoV-2 test for result reporting. And there is a link that we can provide for you that gives you the details on that reporting.

The next question asked, "Do all reporting states require the requesting lab and the reporting, but the performing laboratory report results? Does HHS override this?"

In CLIA purposes, only the laboratory that runs the test must report results.

The next question was asking, "If a state public-health lab refuses to accept a faxed copy of the required results and data, what does CLIA do?"

CLIA cannot speak to how health departments will accept a copy of results. Surveyors will review and verify the laboratory's documentation that SARS-CoV-2 test results were reported to state or local health departments. Please note that the laboratory must have documentation that they made an attempt to report all of the SARS-CoV-2 test results.

The next question asked, "Can you please repeat the reporting requirements for colleges?"

If a college is doing surveillance testing only, which is not covered under CLIA they are not required to report their test results to state or local health departments. However, if a college is doing testing that is screening or diagnostic, then they need to be CLIA-certified, and as such, those test results that they generate are required to be reported to state or local health departments.

The last question that we received was, "We send some results to the state, but we are doing rapid tests in our office. How do we report our in-office results?"

CLIA-certified laboratories must report all SARS-CoV-2 test results to the secretary. If your office is reporting patient-specific rapid-test results, your office meets the definition of a laboratory under CLIA and must report all of those results to the state or local health department. CLIA is not prescriptive in how those results are to be reported, but the laboratory would need to develop their own policies and procedures for reporting the required test results.

And they are all the questions that we did not get a chance to answer last time. So Jasmine, that does it for me. Thank you for the opportunity to be here and talk to you.

JASMINE CHAITRAM: Thank you, Amy. I just wanted to make a comment for the participants on the phone. Many of you out there are curious or are not clear on the difference between diagnostic screening and surveillance testing. I encourage you to visit the CDC website, specifically anything related to laboratory testing. We have, on our laboratory testing page, the definitions of diagnostic screening and surveillance testing. And so that might provide some clarifications for you, and I believe we probably have links for that, as well, in these slides. So Amy, thank you for answering those questions that you received.

FAQs about COVID-19 for Laboratories – Testing Strategies for SARS-CoV-2

So on the last call-- we do have a few more of course on this call. And I'm going to ask you some of those now, if you're good.

AMY ZALE: Sure.

JASMINE CHAITRAM: The first one says, "I just want to be sure that CMS does not intend to fine laboratories who are not reporting all 18 elements required by the CARES Act. What exactly is required to avoid a fine, just the test results? What if no patient-identifiable information is associated with the results? Certificate-of-waiver licenses have no requirement to keep a log of the tests they performed any given day. How can we ensure at a site visit they are reporting if there is no way to verify the tests were performed?"

AMY ZALE: Well, that's a really long question. [LAUGHS]

JASMINE CHAITRAM: Yes. [LAUGHS]

AMY ZALE: I think I'll try to hit the points that I remember. Maybe the ones I don't hit, Jasmine, you can send me, and I'll prepare for next time. But I just want to make it clear that the CARES Act language only requires reporting of test results. It is the HHS guidance that was published on June 4 that actually discusses those 18 data elements. The new CMS laboratory-reporting requirements were only looking for those positive and negative test results.

And oh the CMPs that you're talking about-- the Civil Money Penalties-- are attached to whether or not a laboratory reports all positive and negative test results, and that's all. Now, laboratories are still required to meet the June 4 guidance, and to follow what is outlined in there. But the enforcement piece that CMS is doing is, in our rule, only the positive and negative test results.

JASMINE CHAITRAM: Great. Here's another one.

AMY ZALE: There were a lot of them, Jasmine, so maybe send the other pieces of that question to me.

JASMINE CHAITRAM:

AMY ZALE: Thanks.

JASMINE CHAITRAM: The next one-- "Amy Zale from CMS had mentioned showing documentation that we're reporting to our state or local health department to be in compliance. With this new rule about reporting all results, can we get clarification on what kind of documentation is needed?"

AMY ZALE: So it would really depend on what the laboratory is doing, if you are transmitting things electronically, and there is some kind of log or documentation of that, or email confirmation of that. Each laboratory is going to have their way that they can show that they are transmitting those results.

If you're faxing, you might have the confirmation page from a fax. If you're emailing, there are so many different ways that a laboratory could be meeting this requirement that it's really up to the laboratory to determine how they can best document, and put something in place in their laboratory to show that they are, in fact, meeting this requirement by reporting all positive and negative test results.

JASMINE CHAITRAM: The next question is, "We are an EUA laboratory and perform point-of-care testing in-house. Do we have to report both to local and state, or will our local also report to the state?"

And I can take this one if you'd like, which is that ideally, we would like for the local to be reporting it to the state. But my recommendation is that you contact your local health department, and make sure that those results are also being reported up to the state. But they should be working collaboratively.

Amy, let's see. Let me see if I have another question for you. Just give me one second. Any update on survey guidance for EUA laboratories as mentioned in QSO-20-37?

AMY ZALE: We are working on that as we speak. It's going through our clearance process. So we don't have any definitive date, but it is coming. And we will be putting out-- we have a CLIA Communications Listserv, where we'll be something out on there to let you know it's coming. And we'll be sending it to all the state agencies and, of course, we'll be on this call, too. So as soon as we have that available, we'll let you know.

JASMINE CHAITRAM: Thanks. On the next question is-- this is very similar to the one that I just answered-- "We have been reporting to all local health departments since we started testing, but not to state. Do we also need to report to state and the point of contact, I think."

And so I'm going to say what I said before. It should be sufficient to report to your local health department, but please reach out and make sure that that is correct.

The next one is more of a comment, I think, for CMS and its-- or a request-- to add the publish date to the FAQs on your website.

AMY ZALE: They actually added-- there were two FAQs. One was the university reporting, and one was the point-of-care antigen test reporting, and someone else had made the similar request and that has been added. The effective date has been added at the bottom.

JASMINE CHAITRAM: Thank you. Let's see. Here's one-- "Is only the actual performing laboratory required to report COVID results, or do we need to report all COVID results in our system, even those performed at a reference laboratory who is also reporting?"

AMY ZALE: Now, only the results of the tests that are actually performed in your laboratory. The results that are coming from a reference laboratory are being reported by that reference laboratory. We don't want duplicate reporting. And so it would just be the results of the tests that are formed in your laboratory.

JASMINE CHAITRAM: And I'll just add to that, that I think, again, to check with the state health department that you are reporting to-- I do think that some state health departments do want to have dual reporting from multiple testing sites. So the CDC and CMS feel that it's probably sufficient just to have the testing laboratory report results. But please check with your state health department on their reporting requirements. Let's see here.

"We send be identified samples to the PCR lab. Our reports then come to us de-identified. Of course we are a Phase 1, I think, at our clinical research organization. The lab said that we need to report the results. Is that so? The lab said we should report the results." It's worded weird.

But anyway, so I think the gist of this is that they're dealing with the identified samples. The results are coming back to the clinical research organization. And then the question is, do they need to report the results?

And I'm going to say-- I don't know, Amy, if you want to chime in on this one-- but CDC does have a FAQ specifically for this question on the website. And I do believe that you are the clinical research organization. If you are going to be reporting back results to the individual, then you are supposed to report those results.

But I would suggest that you check the CDC lab reporting web page, and we can add a link to that in the Q&A box here so that everybody can see it and have it. But there is a specific frequently asked question that provides a more detailed answer to that question.

Anything else to add to that, Amy?

AMY ZALE: Not for me. Thanks, Jasmine.

JASMINE CHAITRAM: I think we're going to go ahead and go to our next speaker, and if there is time at the end of the call, and there is additional questions, I'll try to squeeze them in. Thank you so much, Amy for being on the call again today.

AMY ZALE: You're welcome. Thanks, Jasmine.

JASMINE CHAITRAM: So our next speaker is going to be Les Dauphin. She is one of the leads on the CDC Laboratory Task Force, working in the emergency operations center for several weeks now. And she's given us some of her time today to give us some updates and some of the priorities of the Laboratory Task Force. Les?

LESLIE DAUPHIN: Great. Thanks so much, Jasmine. And I'm really happy to join this call. And it has been a little bit more than 60 days since I've been serving as the co-lead for our Laboratory and Testing Task Force and CDC's Incident Management System for the COVID-19 response, so really happy to be here. In my day job at CDC, I serve as the Deputy Director for CDC's Office of Laboratory Science and Safety.

Next slide, please. So just want to give a brief overview of what I plan to share here today. I thought it would be helpful to give a high-level overview of how the Task Force serves in the broader agency response. So I will highlight our mission and our functions, what we're there to do, then some of our priority areas, high-level priorities, and then updates on what we're currently doing, some recent accomplishments, and then some of the ongoing activities, things that will be ongoing for some time. And then, finally, I'll close with some of our plans and next steps.

Next slide, please. Great. So for our mission, I'd like to bucket this, based on how we support public health. It is very much tied into CDC's mission, but specific to the COVID-19 response. Our role as a Task Force is to help increase laboratory testing capacity. And we really do that in a variety of ways. It's through support of public health labs and clinical laboratories, by some of the tools and resources that we develop, such as guidance and also in laboratory support, and

also through engagement. Our engagement with our partners, commercial laboratories, and laboratory organizations.

So that's really, what we as a task force is charged to do. And then we have high-level functions that are really tied into our mission. The way that we carry out our mission is by working in CDC laboratories to develop new tests, new procedures, evaluate new procedures and reagents so that we can develop guidance and share that with laboratories, and then to provide technical support, technical consultation, and to perform laboratory testing.

Next slide, please-- so I want to walk through some of our priority areas, and I've listed them here in three buckets. And these buckets are not necessarily organized in order of importance. So I want to just be clear about that.

The first bucket is around our laboratory studies, research, and development. And so this is the area of the work that really goes on in CDC laboratories, either directly in the laboratory or through collaboration with external partners. Our very top priority right now is to work with partners to assess rapid antigen test performance in the field. And I'll talk a little bit more about that in one of the upcoming slides. And then aligned with our mission to help increase laboratory testing capacity is to evaluate different sample types with our current molecular diagnostic test, to get those validated, and validate new reagents and platforms.

The second bucket is around the support that we can provide through specimens that are submitted directly to CDC for testing, or through the materials that we ship out from our supply, and then also to contribute to laboratories that are performing assessments of reference materials.

And then the final priority area is a big bucket where all of that laboratory work, the research, the engagement, the collaboration, really comes together so that we at the agency and our scientific subject-matter experts are able to provide that technical assistance, and it be available to provide that, also to develop guidance, which comes in the form of guidance as published on our website. It may be frequently asked questions. It may be responses to inquiries, a variety of mechanisms in which we can provide that technical expertise and then field support.

A big part of what we do is to-- and we do it quite often-- is to deploy laboratory scientists out into the field who can really provide technical support for work that is ongoing outside of CDC through investigations and transmission studies.

Next slide, please-- so just a few updates on some ongoing activities I alluded to this an earlier slide, and I want to highlight that the photos in my slide are not stock photos. These are actually real laboratory scientists who were either working in a lab at one time or working in the laboratory now. And my office took these pictures to get folks really in action, and the other images that you see are samples of some of the CDC guidance that's actually published right there on our website.

The one at the top is the interim guidance around antigen testing for SARS-CoV-2, and the one underneath is the interim guidance for pooling, so just to give you an idea of some of the products that are outputs from the work that is ongoing at CDC. So some activities that are underway right now include evaluation of alternate procedures for instruments, including such instruments as automated extraction platforms for reagents that support those that can be used with our currently FDA emergency use-authorized singleplex and multiplex assays, as well as other diagnostic reagents.

Another thing that is really supported by the work in the Division of Laboratory Systems is guidance that is posted at our external website to support laboratory testing, to provide additional information about areas such biosafety, and then additional resources, which I think Jasmine mentioned early in the call, around point-of-care testing.

And then some ongoing activities, which I mentioned-- we are continually working to support testing when specimens are submitted to CDC, and to provide technical support and deployments to the field. Right now, we have several studies that are either in the planning phase or about to begin, where we do have to deploy staff to the field to provide some support.

Next slide, please-- so I want to share with you just a little bit about the priority that I think I mentioned is our top priority, and that is to look at the current FDA emergency use-authorized rapid antigen tests that are currently being deployed or in are in use.

Right now, we as a task force, are really interested in looking at how these commercial products perform, and in settings where they will be used, potentially with people who are asymptomatic. We realize that there is a lot of interest in this area in how these tests will perform. And in order for us to be able to provide some feedback and an informed guidance that may come out around this, we really need to see how the data will be generated.

So a big priority for right for us right now is to establish collaborations and partnerships to learn about how these tests perform. So I just call your attention to the three that we think will be most broadly in use that are highlighted here in this figure, the Sofia SARS2 antigen rapid test, which is-- the manufacturer is Quidel. And it received FDA emergency use authorization in May of this year.

The second is the Veritor system for rapid diagnostics for SARS-CoV2. This is a Becton Dickinson platform, rapid antigen test that received its emergency-use authorization on July of this year.

And then the most recent that there is a lot of interest in is the by next BinaxNOW COVID-19 Antigen Card, by Abbott Laboratories, which received authorization on August of this year.

So the goal here is to really learn about how we can best inform the use of these tests in the settings where they'll be used. And there is a bit of a gap in data, and so we're really interested in seeing how they perform, because we don't know. And so we'd like to continue with forming partnerships and collaborations to see how we can get that done. And this really leads to what I

mentioned one of the previous slides about us deploying staff to the field to support this work in those settings.

Next slide, please-- So I want to close there in the interest of time, and just highlight that there is a lot of work underway right now from the Task Force. We are continuing to work very closely with our partnerships and stakeholders, and other laboratory organizations, as well as within laboratories at CDC to continue to try to do our very best to address some of the critical needs, and form the guidance that gets out to support our public-health efforts.

And with that, I will turn it back over to Jasmine for questions. Thank you.

JASMINE CHAITRAM: Thank you so much, Les, for joining us today and for that great presentation. One of the questions that we got-- and I'll take a stab at it first, and then if you have any thoughts that you want to add, and then also, if Amy from CMS wants to contribute, that would be great-- the question is, "Is there any guidance from CDC on how best to validate or verify the rapid antigen test kits. Some of these come with no known positive or negative control materials."

And so my response to is that the rapid antigen tests that are currently available are considered waived tests and as a waived test, there is no requirement to do additional verification or validation. It's meant to open the box and follow the instructions for use. But I will-- is there anything else you want to add to that, Les?

LESLIE DAUPHIN: No, no, that's it, Jasmine. That will be my answer. I have no more to add there. Thank you.

JASMINE CHAITRAM: Well, let's ask the expert [LAUGHS] at CMS. Amy, what do you think?

AMY ZALE: Well, I agree with what you said, Jasmine. So the only requirement for Certificate of Waiver laboratories who would be using the point-of-care urgent test is to follow the manufacturer instructions, and to report all those test results that we've been talking about. So if there was a validation procedure here in the manufacturer's instructions, obviously, they would be required to do that. In the absence of a validation procedure in the manufacturer's instructions, there is no requirement for a Certificate of Waiver Laboratory to do that.

J**ASMINE CHAITRAM**: Great, thanks. Thanks to both of you. Another question related to antigen tests, "Are positive antigen test results included in the state and national data on number of cases? I learned positive antigen tests with clinical criteria present are considered probable and not confirmed, so are not included in the number of cases. Les, you want to respond to that, and then I can also add?

LESLIE DAUPHIN: Can you repeat that again? Positive within-- I'm sorry. I didn't hear it at all. I'm sorry, please.

JASMINE CHAITRAM: [LAUGHS] That's OK. They're asking about positive antigen tests, and because of the CSTE case definition that they're considered probable, instead of confirmed cases, and the question is, "I think our states and CDC, including that data and the number of cases." And so I can jump in here and say that from what I've seen, it varies across the states. Some states are including those probable cases in their case counts. The information about that should be on their websites. CDC is reporting information that it receives from the states and is trying to do a better job of clarifying where those cases are coming from. And I don't know if you have anything to add to that, Les.

LESLIE DAUPHIN: No, I would just add that right now, this is still not as straightforward as we would hope it could be. There is a great deal of variability, and I know that groups are working very hard to try to get this more manageable. But right now, I think it still varies, unfortunately.

JASMINE CHAITRAM: We got another question. I think it stemmed from the last question we got. And so, Amy, this one, I think, will be for you, just to continue to clarify on this topic. It says, "So for waived tests, a CLIA lab does not have to verify validate waived systems."

LESLIE DAUPHIN: It has to follow manufacturer's instructions, and so whatever the manufacturer's instructions tell the laboratory that they need to do is what the arbitrary; laboratory needs to do. There are so many ways that I don't know specifically, whether or not they have verification or validation panels with them.

And if they do, obviously, the laboratory would be required to perform that. But if they don't specifically require it in the manufacturer's instructions, and a Certificate of Waiver Laboratory is only required to follow what's in the package insert.

JASMINE CHAITRAM: Thanks. And Les, here's another one for you, "Will the CDC influenza SARS-CoV-2 multiplex assay include the KingFisher instrument in the one option of RNA extraction in the future?"

LESLIE DAUPHIN: I do believe the KingFisher is one that is being evaluated, but I can verify that. I'm almost positive but I'm not 100% positive. And we can get that answer back to you, Jasmine to share.

JASMINE CHAITRAM: That would be great, thank you. In the interest of time, I'm going to go ahead and move to our last speaker for today. We always have an update from the Food and Drug Administration, from Tim Stenzel. And I feel like Tim is always running short on time, because of where he is in the agenda. So I'm going to give him plenty of time today to answer the questions that I've provided to him from a previous call. And then, Tim, we have already gotten questions live today, that hopefully you can answer a few of those, as well.

TIM STENZEL: Thanks, Jasmine. I'll do my best. And as usual, It's good to be on the call, and also, we usually have some good, challenging questions. First question is, "What are the new priorities for emergency use authorization? Our EUA went from being a high priority to a low

priority without any clarification on what caused the change." Personally, I would-- this is Tim speaking-- I would need to know the specifics to be able to give you a specific response. So if you want, you can send an email to our CDRH-EUA-templates@fda.hhs.gov for more details specific to your application.

As we have stated previously, though, we generally prioritize tests that are not able to be offered prior to or without an EUA under other policies. And, therefore, most tests that get submitted to us can go to market without getting an EUA authorization, and we take that strongly into account when we set priorities. And if new submissions are made, and they are high priority, they do go ahead of those that are high priority that-- and I'll go through some of those. They do go to the head of the line.

And so specifically, we have been prioritizing, and it can shift a little bit through this pandemic. So right now, we're prioritizing, pooling additions to commercial test reagent kits, and that's because so many different labs can use these kits, and, therefore, they don't have to do their own validations for pooling. Point-of-care tests, home collection tests, at-home tests, or what we have previously called non-lab self-tests, multi-analyzed tests-- these are, in particular, ones that add to a SARS test of flu A and B, or add SARS to a previous panel, and then also high throughput distributed tests.

And these probably have pretty good obvious explanations for why they're high priorities. But even with those priorities set, due to the very high volumes of EUAs, and we are still getting significant new applications, even now, even some of those high priorities applications have yet to be assigned a lead reviewer. And we want to move those through as soon as possible. And so that does, unfortunately, require that prioritization.

Those that aren't assigned yet a lead reviewer are assigned to point of contact within our office to be able to give weekly updates. Tests that are not currently assigned to the lead reviewer, but fall into a priority category, will be among the first to be brought back to the reviewers' cues when we have that review capacity.

Also I'd like to say that if there is any data that we've requested and we're waiting on, those applications are typically triaged back to that assigned contact within our office until that data is received. Due to the volume of submissions and the continued high-volume communication on an application that is waiting, further data does slow up a review process. And other applications and those waiting to be assigned a reviewer can be delayed. So for that reason, we are moving those off the reviewers' queue when we're waiting on new data that has been requested.

Moving on to the next question, "The saliva test used at Yale has approved based on results for patients with diagnosis of COVID. The usage is just stated for symptomatic patients suspected of COVID. How can this be used for screening college students who are asymptomatic?" So SalivaDirect was authorized for individuals suspected of COVID-19 whether or not they are symptomatic. Individuals may be suspected of COVID-19 for reasons other than being

symptomatic. While it is not authorized for asymptomatic screening, at least at this time, health-care providers may order it off-label label as described in our FAQs on the FDA website.

Next question-- "Is there a website that informs us which COVID tests have been submitted to the FDA and are pending review, a pipeline of tests that may soon be available?" The FDA is not able to release this kind of information about tests that have been submitted, and that have not been issued a final decision, due to confidential issues. However, developers themselves are free to provide updates, and we don't interfere with that. I would also say that if anybody has notified and is then is posted on the website, there is a time limit between when they notify the FDA and when they are required to submit their EUA submission. So if that time has passed, and they are still on the notification list, then you know it's a pretty good assumption that they've submitted their data, and it's under review in some capacity.

Next question-- "Is there an update for the BD Max SARS-CoV-2 reagent for higher positivity rate?"

I think this may be in regards to a previously discussed issue having to do with an increased false positive rate. If so, we have updated the intended use for the BD, SARS-CoV-2 reagents for the BD Max system, and includes language, "Positive results should be treated as presumptive and should be tested with a different authorized or cleared molecular test."

I am not sure what we can say beyond this moment, other than to say that any developer that has a reported issue, we work very closely with them to resolve that. And as soon as we do, we'll make that public.

Next question-- "Does FDA currently have a backlog of the EUA applications for COVID-19? How many are currently pending? What is the current average time from application received to decision?"

Yes, we currently have a backlog. The FDA has received an unprecedented number of EUA requests, on top of our normal work, and which continues, and is working through reviews as quickly as possible. The time to decision does vary greatly, depending on the priority. Also, as mentioned earlier, there is a notification pathway for most tests into the market. And so that does allow us and the developer to advanced care within this pandemic in a much more rapid manner.

Our next question is, "What LoD would be considered an infective level of virus?"

The correlation between viral load and infective virus is not well established or understood. LoD is the minimal amount of virus detectable by an assay, and it is unknown what specific LoD correlate with infectivity. Further, without an international standard, it is more challenging to gain this information. With the FDA reference panel data now published, and more data will be published on a regular basis, perhaps correlations can be made between assays and with outcomes to help inform them.

I would note that we have seen multiple examples of symptomatic patients-- those are patients with symptoms-- in the first five to seven days of infection and have very high CTs, even as high as a CT of 40, or 0.40.

Next question-- "Will all sputum assays have the caveat to retest negatives with a different molecular assay, if deemed important for patient management?"

I know this is not a standard limitation for sputum, as it is a routine claim specimen type for SARS, so there is no requirement to retest negatives.

Next question-- "Is FDA ready to approve at-home rapid," it says, but, "self-administered rapid tests that will not require a prescription, a test that is a daily paper test that is very low cost and is for asymptomatic people."

So we usually refer this to OTC or over-the-counter. Yes, so though we have not yet received a single home test EUA application. That includes both by prescription, or for OTC. The FDA, however, is working with a number of developers-- I have a number of those conversations on a regular basis-- including those funded by the RADx program. We do evaluate every test individually, considering the totality of evidence, and look at the overall benefit-risk calculation.

The FDA does support any testing proposal where, among other criteria, the benefits outweigh the risks based on sound science, and is ready to authorize these tests and others. You may have noted in my piece in The Hill a couple weeks ago, which explicitly expressed flexibility with regarding authorizing such tests for use in a home or in non-lab settings, including the use of serial tests to up the performance, if performance is not able to be authorized, based on the results of one test.

We do think it's important to capture the bulk of those who are infectious, with an overall positive result. As I mentioned earlier, we are seeing people in the first few days of symptoms who have very high fatigue. So it's a bit challenging to develop such a test if it doesn't actually perform well in that period of time.

The next question is, "You mentioned there are no EUA for home collection," then they noted that there are 23 entries for home collection on our website.

Yes, there are many EUAs ways for home collection that have been authorized. However, to clarify perhaps what I said or someone else said, there are currently no EUAs for tests to be formed fully at home without a specimen being sent to the lab.

"For antigen tests, if the first test was negative, when do you recommend retest again for antigen tests?"

If there is a high suspicion for the first test being a false negative. So I would say there isn't a firm recognition of reflexing a negative antigen test. However, if the clinical suspicion is high it's

up to the ordering clinician to make that assessment, and then reflex to a molecular test that's high sensitivity would be wise in that situation.

Next in the last prepared question is, "Given that HHS has said LDTs no longer require FDA approval. Does that mean that self-collection devices for LDTs do not need FDA approval, either?"

It is unclear to me if the collection swab is considered a device or part of the LDT. Collection devices are not considered to be LDTs. LDTs are tests designed, manufactured, and used within a single CLIA-certified laboratory. This does not include, for example, test components, such as collection devices, platforms, and reagents, nor does it refer to home-collection tests, at-home tests, direct-to-consumer tests, over-the-counter tests, tests distributed or used beyond the single laboratory in which it was developed, or tests designed in one location, but manufacturer and/or used in another location.

So that was a lot of questions and answers. Back to you, Jasmine.

JASMINE CHAITRAM: Thank you, Tim, for providing those answers. Before I ask you the questions from this week, I did want to squeeze in just one clarification on reporting, since we got a lot of questions about reporting to locals versus state health departments. I do want to remind all those participants on this call that one thing about reporting is that you should be reporting to the state in which the patient resides. So if you have an out-of-state person, you shouldn't be reporting that result to the local health department. That should be going to the state where that person came from. And I'll go ahead and let you all know that our next call, on October 19, we're going to talk more about reporting. And so if your questions were not answered today, or if you have additional questions, please plan to join us on October 19 for more information about reporting.

The question I have for you, Tim, "Is the BinaxNOW antigen IFU states that negatives are presumptive for patients tested after the seven-day period from onset. Does that mean negative results within seven days of onset are confirmatory?

TIM STENZEL: That's a great question. This is the antigen test, right? The BinaxNOW?

JASMINE CHAITRAM: Yes.

TIM STENZEL: I would say that the same language that applies to every other antigen test we've authorized would apply here, that if you get a negative result within the time period, or after the time period, use good clinical judgment to determine if a follow-up alternative, such as a high sensitivity molecular test, would be appropriate. And I will review that IFU language to see if it doesn't need any tweaking.

JASMINE CHAITRAM: "If EUA's intended use is for symptomatic patients and is being used for asymptomatic persons, is that then no longer an EUA test but high complexity in the long-term care setting, with a clear certificate of waiver in particular?

TIM STENZEL: So this is also a question that can be answered by CMS. But from an FDA perspective, it's entirely OK for clinicians to order a test off-label, and for labs to perform that testing and report that result. I don't know if CMS is on and can comment, but it's my understanding that they have provided the OK that these tests, even though they don't have a claim for a symptomatic indication yet, can be used in this situation.

JASMINE CHAITRAM: Another question was, "Do all"-- oh, sorry, Amy, did you want to chime in on that one? Go ahead.

AMY ZALE: I missed the question, initially, but it sounded like the talk was about the point-of-care antigen testing and it being done on asymptomatic individuals. Is that correct?

TIM STENZEL: That's correct.

JASMINE CHAITRAM: Yeah, and then-- yes.

AMY ZALE: So we actually have an FAQ out that talks specifically about this, and we have said that CMS and the CLIA program is exercising enforcement discretion when it comes to asymptomatic testing with the point-of-care antigen test, and that Certificate of Waiver Laboratories who are performing a point-of-care antigen test will not be cited if they are testing asymptomatic individuals.

TIM STENZEL: That's perfect, I think. Thank you.

AMY ZALE: Sure.

JASMINE CHAITRAM: Thank you. Here's, I think, a short and easy one, "Do all VTM manufacturers need FDA approval?"

TIM STENZEL: No. We have provided guidance around VTM. So go to the FAQ page and the guidance document on VTM and see if it applies to you in your situation. If it doesn't, we're always willing to take questions at our templates email address.

JASMINE CHAITRAM: Thank you very much, Tim, and thank you to all of our panelists today. We're right at the end of our hour. I want to thank all of our participants, as well. And I also want to just take a quick second to thank the Division of Laboratory Systems team that helps to put on all of these calls. There's a lot of folks that do help make these calls happen, so thanks to them as well. Reminder to sign up for LOCS emails if you're not already receiving them. That's LOCS@cdc.gov. Our next call will be on October 19. Thank you for joining us today, and stay safe.