Clinical Laboratory COVID-19 Response Call
March 22, 2021

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JASMINE CHAITRAM: Hello, everyone, and thank you for joining the Clinical Laboratory COVID-19 Response call. Apologies for starting late today. We were waiting for a few of our speakers to join us. I'm Jasmine Chaitram. I'm the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems.

The Division of Laboratory Systems has been hosting these calls since March of 2020, so it's been a little over a year since we've been having these calls. And we really hope that they've been useful to you. I know some of you have written emails to me and said that you do appreciate the calls, and I thank you for that feedback. We also welcome negative feedback, too, or ways to improve these calls or topics that we should include in future agenda items. So feel free to send those to locs@cdc.gov. That's locs@cdc.gov. And I'll talk about that a little bit more in a minute.

I do want to cover a few items about the Division of Laboratory Systems. Just a reminder that we have been providing information to clinical and public health laboratories before COVID on a variety of topics, including quality and safety, training and workforce development, biorepository science, data science and informatics, as well as preparedness and response efforts. And we continue to do that in our role here in the COVID-19 response, serving as a liaison between the clinical laboratory community and the CDC Emergency Operations Center.

I've listed here our agenda for today's call. And I'm going to actually go through a couple of announcements before we get into our speakers. First up is that we have a new webpage called Testing Strategies. And this is not new information, but we did pull it out so that it's a little bit more clear and

easier to find. This is information about diagnostic testing, screening testing, and surveillance, and the difference between the three. And it includes information about reporting whenever you're doing this type of testing, as well as the CLIA requirements.

Our Point of Care webpage has also been updated recently. We added additional training resources for new point-of-care tests. And importantly, we've added information about obtaining a CLIA certificate of waiver, and that you can begin testing and reporting as soon as you submit your application to the state agency, as long as there aren't any additional state license requirements that also apply. So that's for those of you that are performing point-of-care testing.

And we also updated our Antibody Guidance Testing page. And we have information on that page about-- recently updated information about available serology tests. We've also provided guidance about performance of tests on individuals that have been vaccinated for SARS-CoV-2. And we've also provided some additional guidance for seropositive individuals, and whether or not they need to quarantine after they've been exposed to someone with suspected or confirmed COVID-19.

And a reminder that all of DLS preparedness-related information is on our Preparedness Portal. Here, you can also find links to our Clinical Lab COVID-19 Response calls. We call them CLCR calls. And there, you can find recordings, transcripts, and presentations from all of our previous calls. You can also find all of the LOCS messages-- that's the email distribution we use to provide guidance-- any other updates from other agencies, as well as announce these calls.

And you can send emails to locs@cdc.gov with any questions that you have, and we can respond to you there. We also have important messages archived on our website. And we have links to other preparedness information. So this is kind of a one-stop shop and go there if you are looking for anything in particular. Hopefully, you can find it.

The next call will be on Monday, April 5th from 3:00 to 4:00 PM. We host these calls every other Monday. And our Training and Workforce Development Group wants to hear from you, so please submit any questions or suggestions about education and training needs to labtrainingneeds@cdc.gov.
Asking a question, please remember to ask a question using the Q&A button in the Zoom webinar system. This should be at the bottom of your screen and is a Q&A box. We really don't want you to submit your questions through the chat. It's hard for us to track them there. When you are submitting a question, and if you're willing to, please include your name and email address.

We try very hard to answer the questions live, but because we get so many questions during these calls and we have so many speakers and a limited amount of time, we sometimes have to answer these questions either offline, through email, or in a future call. And so having your email address helps us to get back to you if we're not able to answer your call today. For media questions, if you are the media, this is not a call intended for the media, this is a call intended for clinical laboratories and testing facilities. So if you are the media, please direct your questions to media@cdc.gov. And if you're a patient, please direct your questions to your health care provider.

And then lastly, I just want to note that the slide decks may contain presentation material from panelists that are not affiliated with CDC. So just be aware that this information does not necessarily reflect CDC's official position. And as I mentioned, these presentations will be posted on our Preparedness Portal, so the same disclaimer applies to information posted there.

And with that, I think we're ready to go into our first topic, which is going to be Vivien Dugan from the CDC Laboratory and Testing Task Force giving an update on the SARS-CoV-2 variants. She's been doing this for the last three weeks-- or the last three calls, rather-- and we really appreciate her being here. Thank you. Vivien.

VIVIEN DUGAN: Thanks, Jasmine. OK, and go to the next slide, please. Good to be with you all again. Going to give some updates on variants, just some new data and new information that we've posted on our website. So on our Variant page, we've added variant classifications. And so these were essentially established in collaboration with our interagency group, called the SARS-CoV-2 interagency group, the SIG, where we have representatives from CDC, NIH, FDA, DoD, BARDA, USDA, and I'm probably forgetting one or two other groups. And so each of these classes essentially include possible attributes of lower classes. And so the variant's status may escalate or deescalate based on the scientific evidence that's available.

So the way we think about these and we've tried to organize them as we talk about variants of interest, variants of concern, or variants of high consequence. And so for each of these there's some type of impact and evidence for-- different types of evidence for how these variants either impact neutralization by antibodies, efficacy of treatments, impact or disease severity, and also, of course, any impact on the vaccine.

So variants of interest-- and there's more data on our web page, so I certainly encourage everyone to go there and look. But the variants of interest essentially contain genetic markers that have an association with any of these impacts or are predicted to have an impact. Variants of concern have evidence of increased transmissibility, and again, impacts evidence where they impact all of these different factors, or one or more of these factors. And then, variants of high consequence have clear evidence that prevention measures or medical countermeasures might have significantly reduced effectiveness relative to previously circulating variants.

So there are more data on our website page. I certainly encourage you all to check it out there. But this is just kind of a high-level classifications that we have put out there as of last week. Next slide, please. So some more data on that page. We've classified some of the variants of interest that you may be hearing about or be familiar with. The B.1.526, which is the New York variant that was first detected in New York. It has several different markers in the spike gene, the E484K, a number of these B.1.526 viruses that are co-circulating with other ones. So there's kind of a lot of diversity within this B.1.526 lineage.

There's also the B.1.525, first detected in New York, also shares E484K with some of the B.1.526s. And then the P.2 variants, and so those are-- sorry, I'm having a hard time seeing. So the P.2 was first detected in Brazil in April 2020. And so you can see that some of the predicted attributes are listed there in the last column. Next slide, please.

OK, I'm hearing maybe that my volume isn't loud enough, so I'm going to make that louder. Hopefully that helps. OK. These are listed variants of concern. Again, these viruses or variants are listed on our website page. The B.1,17, first detected in the United Kingdom, the P.1 and the B.1.351, I believe that you're all familiar with. The B.1.427 and the B.1.429 were recently classified as variants of concern. You can see here, their known attributes.

Really, the main reason-- and I will let FDA probably talk about this a little bit more, but they have moderate reduction in utilization using convalescent and post-vaccination sera, and there's a significant impact on neutralization by some, but not all EUA therapeutics. And so those two B.1.427s and B.1.429, first detected in California, and they contain that change in the spike gene, that 452R. Next slide, please. Next, we're going to show some of the national SARS-CoV-2 variant proportions. So this is a new page that we added to our website. It's pretty easy to find, linkable, but we can add the link in the chat as well. And so these data are a little bit more updated than the data that are currently on there. And essentially, this shows the different proportions of the top circulating, or most prevalent circulating variants by lineage in the US. So if you look at the left side of the graph, there are these bar charts. And that's a rolling 12-week period.

So each bar chart shows a two-week interval of specimens collected, with the date listed at the bottom being the last date. So for example, the first bar chart is January 2, 2021. So two weeks prior, it's all the specimens collected two weeks prior to January 2, 2021.

So you can see the different proportions of the variants of interest and variants of concern, as well as this other garden variety SARS-CoV-2 viruses that are also circulating at the national level. Again, this is all national data, looking at all the data that CDC has either generated or has received from contract labs. So these are contract labs that we've funded to enhance a lot of our representative surveillance for specimens that are less biased than, say, some of the other data that may be out there in the public domain.

So if you look at the key or lineage key on the right-hand side with the numbers, we've got, again, a breakdown of all the co-circulating top variants, at least at 1% circulating across the US. And if we go down from top to bottom, and so you can see that each variant of interest and variant of concern are listed here. And so overall, that B.1.17 is increasing nationally, the B.1.427 and B.1.49, originally detected in California, those are also increasing nationally.

But when we look at other variants of concern, the B.1.351 and the P.1 at the bottom of that chart remain well below 0.5%. And so when we look at that lineage key data, that represents the data and the bar chart

from February 13 and the two weeks before, combined with the February 27 data and two weeks before. So it's four weeks total of when the specimens were collected.

And the reason why we do that is because a lot of the data in that March 13 bar chart, that's still changing. We're still getting a lot of specimens in that were collected at that time, and the sequence is coming in now. So this is how we're trying to get a better picture, a more stable picture of what's circulating nationally. Next slide, please.

OK, and I think this is last but not least. We also, on the same variant proportions in the US page, which is a new page, we've added state-level SARS-CoV-2 variant proportions. And we expect these data will change along with the data on the last page, or the last slide. We plan to update this on a weekly basis. And so this new state-level variant proportion data is essentially the same baseline of data. So it's CDC sequence data from our national SARS-CoV-2 strain surveillance network as well as our contracts that we funded to enhance a lot of that baseline surveillance of representative specimens. And this data is also four weeks, ending February 13-- it's a little bit earlier. We are going to update this as well.

And so again, these are when the specimens were collected, February 13 and 4 weeks prior. We have the variant of concern proportion estimates for each state. And this is not for every state. Essentially, we wanted to see, do we have sufficient data at this point to look more granularly at the state level?

And so right now our system was built at the national level. But it turns out with a lot of our enhancements we are able to look at the proportions of variants of concern at the state level. So right now, we have 19 states listed. They've got the proportions for, again, all the variants of concern, all five of them.

And based on this data, the US government chose to set a threshold of a 20% prevalence of that California variant, the one that was initially found in California with the L452 change to guide distribution of one of the EUA therapeutics, bamlanivimab. And so this action was really going to only affect the states of California, Arizona, and Nevada. And so this is based on some of the data that we've been able to provide in support of these decisions.

Currently, we, at CDC, we're not requesting any of these particular variants be reported. We are detecting them through our national strain surveillance. We have a pretty good idea of where they are, and we show got data on the state level proportions. But if that guidance changes or anything changes, we will certainly notify our jurisdictions and partners.

So you can see some of the proportions down there on the bottom, but I certainly encourage everyone to check out the information, as it does relate to some of the FDA notices that have been come out recently. I think that's all I have.

JASMINE CHAITRAM: Thanks, Vivien. I did have a question for you that came through. And the question says, can you comment on the clinical significance of the R.1 variant? We have seen a couple of these

pop up recently, and GISAID also shows this variant taking off. There's scant literature, so clinical insights are appreciated. Thank you.

VIVIEN DUGAN: And see, the lab doesn't really do clinical insights, so I appreciate the question. Certainly, it's a virus that we have detected and it's part of what we're getting in, again, as getting baseline specimens. We want to get a diversity and a good picture of what's really circulating out there. So we do have some of these specimens in-house.

I believe the R.1s have the 484E to K change, so they're one of the many viruses that do have this change. They have a couple of others. And so I think we're starting to see a little bit more of these viruses change in proportion, but they're not making our top list at the national level just yet.

But we're certainly keeping an eye on them to see if they're increasing in proportion and, of course, depending on a lot of the state-level and jurisdictional-level data to see what's happening out there, if it is increasing in more of a regional location, kind of how we're seeing the California and New York type diversity changing. So we're keeping an eye on it for sure. And if we get any more clinical insights or insights on the virologic side, we'll certainly let people know.

JASMINE CHAITRAM: Great. Thank you. One more question for you. The nomenclature for SARS-CoV-2 variants is not well-standardized. Some labs and organizations call mutations variants and refer to lineages such as B.1.1.7 based on the mutations that define them. Now it seems that CDC refers to these lineages as variants. Will CDC, WHO, or anyone else involved sit down and standardize the nomenclature?

VIVIEN DUGAN: Yeah, I think that there are efforts to do that, certainly from WHO as far as, there's a couple of different ways. So there's the whole classification side. So I believe WHO has some working definitions on what they're considering variants of interest versus variants of concern.

But then, there's also the more academic nomenclature when you're submitting a lot of these viruses or talking about them. And I think it really depends on what your level of interest is in how we talk about them now. So for now, CDC is referring to most of these on our website as lineages, although noting that a lot of these different lineages will have different diversity as far as different substitutions or mutations that tend to define the lineage through a common ancestor. So I think, going forward, we hope to have more information, at least as we're working with WHO. But it is a challenging space, for sure.

JASMINE CHAITRAM: Vivien, thank you so much for being here today. I know you're super busy and I appreciate your time.

VIVIEN DUGAN: Thanks.

JASMINE CHAITRAM: OK, we're going to our next speaker. We've actually got two individuals from the University of Illinois. And the presentation is going to be longitudinal comparison of multimodal

coronavirus test results with live virus shedding. And I believe that our first speaker is going to be Christopher Brooke. Christopher?

CHRISTOPHER BROOKE: Yep, hi. Thanks for having us here today. So my name is Chris Brooke. I'm a faculty member at the University of Illinois Urbana-Champaign. And I want to talk about a study we've been running for the last few months now called COVID Detect. Can I get the next slide, please?
So because there's not a lot of time, I want to kind of move quickly. So there's two main goals to the study. The first is to quantitatively compare the performance of different diagnostic testing methods over the course of acute SARS-CoV-2 infection. And this is just because this image here that's shown on the bottom is kind of hypothetical.

We don't really have the data to understand what viral dynamics look like in infected individuals, and thus, how different tests with different sensitivities perform at different stages of infection. And so that's the primary goal of this study is to get longitudinal data from people that we capture very early during infection, both to generate a high-resolution description of acute infection dynamics and to use that information to quantitatively assess sensitivity of different tests at different stages of infection. Can I get the next slide, please?

Just really quickly, the study is enabled by a large-scale screening system that we have in the University of Illinois campus. It's enabled by direct saliva to our RT-qPCR assay that we developed in-house and now has EUA approval, and we're basically running 10,000 or more tests a day. So everyone on campus is screened at least twice a week using this test. So can we go to the next slide, please?

And this is important because it allows us to capture people very early during infection. And so the study participant pool that we're working with comes in two categories. The first are people who are within 24 hours of their first positive RT-qPCR test. I should point out that our results reporting is very rapid. It's typically well under 24 hours, often under 12 hours.

And so we're enrolling people within the first 24 hours after their first positive COVID test. So that's the bulk of our participants. We are also enrolling people who are quarantining due to exposure to a known positive, with the idea here that a percentage, in our hands it's around 10%, will test positive while they're enrolled. And so we'll get to see the entirety of the curve.

But so these are two main pools of participants. I should also point out that eligibility requires that people have had a negative test result on campus within the last seven days. So we're really trying to avoid enrolling people who are kind of at the tail end of infection.

Once they're enrolled, we do daily sampling for 14 days, or up to 14 days. We're doing our EUA saliva RT-qPCR test, which is called COVID SHIELD. We are doing nasal swabs for both our RT-qPCR via the Alinity assay and for the Quidel Sofia SARS antigen FIA. And then, we are also looking at viral infectivity from nasal swabs using a cell culture assay, so we can tell what days people have live virus, infectious

virus detectable nasal swabs. OK, so we're doing this every day for up to 14 days. Can I get the next slide, please?

OK, and this is just a representation of the sorts of data that we're capturing. So this is one individual. And we're showing nasal qPCR CT values in the blue dots, saliva the qPCR CT results on the green dots, infectious virus in red x's, and then antigen positivity, by the Quidel is the yellow blocks. And the point here being that we're seeing both the rise and fall of viral shedding here, so we're really capturing many of these participants very early during infection so that we can actually see how tests perform before they're even shedding detectable levels of infectious virus.

OK, can I get the next slide, please? OK, so I'm going to hand things over to Becky Smith, who is co-PI on this project and has been doing the analysis comparing different test sensitivities. I should have pointed out in the slides that we have a preprint on that archive that came out a couple of days ago that has these data. And I can drop that link into the chat. But Becky, do you want to take over here?

REBECCA SMITH: Sure. Thank you, Chris. So one of the things that we really wanted to do was align these samples by time. And there's a lot of different ways we could do that, but we decided to align them for this analysis by the days since first viral culture, so the first time that we were able to culture the virus out of these nasal samples.

On the left hand you'll see the daily sensitivity. So per day, what proportion of these infected individuals were detected by the different tests, with the top being the antigen test from Quidel, the middle being the Alinity nasal RT-qPCR, and the bottom being our in-house COVID SHIELD test with saliva direct RT-qPCR.
And you'll see that the RT-qPCRs are much higher before the viral culture becomes positive than the antigen test, but all really peak in sensitivity at the time that the viral culture becomes positive. And the antigen test falls away fastest afterwards, and the nasal and saliva also fall away, but much more slowly, especially with the nasal. On the right hand we looked at just breaking that into the categories of the four nasal culture positive, which is the pre-positive set where you see that we've got 60% to 80% sensitivity in the RT-qPCRs and under 40% sensitivity for the antigen test, to the positive time, this is when there is a synchronous viral culture positive where you see we have very high sensitivity in all the tests.
And then, post-positive is when they have had a viral culture positive but are no longer viral culture positive. And you see that the sensitivity of the antigen test has dropped down to about 50%, but the sensitivity of the RT-qPCR stays fairly high, although not as high as when the viral culture was still positive. The next slide, please?

We also looked at how these test results would look if we did different frequencies of testing, from daily to weekly. And we asked, what proportion of these people on a particular schedule, with a particular start date, would we have detected using these frequencies? And on the right, you see the probability of detecting infection at any stage, so detecting any infected individual.

And again, as the frequency decreases, the sensitivity of the test decrease. But they're all very high. Every single test found every individual if you tested daily. On the left-hand side, though, is looking at the probability of detecting them before or during their viral culture positive time. This is what we consider, potentially, the infectivity time.

And you can see that for all of the tests, that sensitivity drops quite dramatically as we decrease our frequency. And it drops at almost the same rate for all three of the tests. So we don't really see an advantage to any of the tests, whereas when we're looking at detecting the infection at any stage, the frequency of testing matters a little bit less for the highly sensitive tests, RT-qPCRs. Next slide, please.

So our conclusions are that the RT-qPCR is more sensitive than the Quidel antigen assay prior to and following the period of viral culture positivity. All the test modalities peaked in sensitivity during that period of viral culture positivity, and that screening at least twice a week using any testing modality, will give a sensitivity of about 95% or greater for detecting infection, but the higher frequency testing is important if you want to identify individuals prior to or during the infectious period. Next slide.

And this is the entire team involved in the project. It's required a lot of people working very hard. So we're very thankful for all of the help that we've had working on this project.

CHRISTOPHER BROOKE: Yeah, as you point out, this is under the broader umbrella of the Clinical Studies Corps at UMass Medical School. It's been funded through the NIH RADx tech program via NIBIB and HLBI. There was a question earlier about qPCR tests. They're all done in CLIA labs. The saliva test is done in our on-campus CLIA lab. The nasal RT-qPCR test is done in a CLIA lab at Johns Hopkins. And the antigen test is run at Carle Foundation Hospital's lab, which is right down the street.

JASMINE CHAITRAM: Thank you, Chris and Becky. And thank you, Chris, for answering some of the questions in the Q&A box. Appreciate that. I think there was another question that kind of came through the chat, and it was about high throughput antigen tests. Have you guys looked at that or plan to?

CHRISTOPHER BROOKE: The only antigen test we had looked at in the context of the study was the Quidel Sofia. So we're not comparing across different antigen tests.

JASMINE CHAITRAM: OK. All right. Well, thank you. I don't see any other questions right now, but you're welcome to stay on, and if other questions pop up and you want to answer them in the Q&A box, we do appreciate that. And we do appreciate you being on today and giving this great presentation. So thank you.

CHRISTOPHER BROOKE: Thanks for having us.

JASMINE CHAITRAM: All right. Our next topic is a CMS update. We've had a few of these before. We have a new speaker today, though. It's Monique Spruill from the Centers for Medicare & Medicaid Services. Monique, we didn't get to do a sound check, so I hope the sound is OK. You may be on mute.

One more time, Monique, can you unmute yourself and talk? As a backup plan, we also have Amy Zale from CMS, who has been on these calls before as well. And perhaps, Amy can give the CMS update today.

AMY ZALE: Happy to. Thanks for having us, Jasmine. Hi, everyone. Thank you for everything that you're doing. We really appreciate it. I wanted to let everyone know that we have an FAQ that was just released on Friday. So we had one that was initially released, we got stakeholder feedback that it was problematic for some people. And so we revised the FAQ, and it was republished on Friday.

And we just wanted to let you know that CMS is temporarily exercising enforcement discretion, to say that laboratories or facilities can report variate results to public health departments for public health purposes, without being CLIA-certified.

I just want to stress, that if any of those results are being reported for the purpose of diagnosis, prevention, treatment of that individual. Or if the result is going to be returned to the patient, or to their health care provider, then the facility needs to be CLIA-certified. That is the gist of our FAQ. And I will take any questions that you have at this time.

JASMINE CHAITRAM: Thank you so much, Amy, for stepping in and giving that update. I think the revision to the FAQ is very helpful. And we appreciate CMS doing that. And we did send out a LOCS message today before the call, which announced the FAQ. And so hopefully, the laboratories were able to see that and got a chance to read it.

And I am not seeing any questions specifically about the FAQ at this time. So if you want to hang on. And if any of them come up, I can either ask you-- Oh, here's one. Let's see, Amy Zale, can you help understand the difference between reporting to LHD? I'm not sure if they meant state health department. And then who does contact tracing? Hence, notifying the patient and the physician. So the difference between reporting to the state health department versus contact tracing. She's saying local health departments. Thanks. And who gets to do the contact tracing once it's reported?

AMY ZALE: Sure. And so the first thing that I would say, is that CMS and the CLIA program only has oversight over laboratories. And so what happens from the public health department perspective, is out of our oversight. But I would say that if they are doing contact tracing, they are using that result for epidemiological purposes, that is where we're giving our enforcement discretion.

And if they [the laboratory] are giving that information specifically to a patient, or for diagnosing that patient, or to modify treatment for that patient, then that laboratory has to have a CLIA certificate. Otherwise, as long as it's for public health purposes to include contact tracing, that can be done in a non-CLIA certified laboratory.

JASMINE CHAITRAM: Thanks, Amy. Can you elaborate a little bit more on the public health department's ability to report results to the patient?

AMY ZALE: So I can't speak a ton on the public health department side, because that, again, is outside of CLIA's oversight. Our oversight stops when the laboratory reports it to the public health department. What the public health department does with that information, as long as it's being used for public health purposes to include contact tracing, then CMS is not going to take action against that laboratory.
But again, CMS does not have oversight over the public health department, and what they do with that information for public health purposes. But if the result is [intended to be] returned to the patient for the purpose of diagnosis, or for treatment, or prevention of disease, then that laboratory needs to have a CLIA certificate before they can send the result to the public health department.

JASMINE CHAITRAM: Thank you so much, Amy. And we had a question in the Q&A box about the link for the FAQ. So we are going to get that in the chat in a couple of minutes.

AMY ZALE: I can actually add that to the chat box, Jasmine.

JASMINE CHAITRAM: That would be great. So I guess one more question here, if we are a CLIA but have not validated the sequencing assay. And we are relying the information to the public health department, that is then relaying the information to the patient and the physician that may impact treatment, is that acceptable?

AMY ZALE: If the health department is relaying that information to the patient and their practitioner [as intended by the laboratory], for diagnosis or for treatment purposes, then the laboratory needs to have a CLIA certificate, and they need to follow all CLIA regulations.

JASMINE CHAITRAM: Can I ask you a non-reporting question here? Hang on, I just saw it. I just added the link to the chat.

JASMINE CHAITRAM: Wonderful, thank you. With CLIA waivers being easier for entities to get, how would that affect other CLIA laboratories who may be owned by the same company or individual, if the new CLIA waiver holder does not follow the guidelines? It's a tricky one. You may want to just look at that one. It's in the Q&A box. Think you're on mute.

AMY ZALE: I am on mute. Thank you. What time did it come in? I'm not entirely sure I understand what that question means.

JASMINE CHAITRAM: That one's coming-- I'm not sure I understand either. So 3:39.

AMY ZALE: Let me see if I can take that one.

JASMINE CHAITRAM: But think it's for when a facility has a CLIA waiver, that's been extended from someplace else. But I think if we're talking about reporting for the variants, that's not going to be done in a CLIA waiver facility.

AMY ZALE: Correct.

JASMINE CHAITRAM: Anyway, I'll let you look at that. And you'll handle it, you're the expert. So thank you for being on and answering some of these calls. And stepping in to talk about the FAQ.

AMY ZALE: You're welcome. And yes, I would agree with what you said. How I'm looking at this, I would be surprised if a CLIA Certificate of Waiver laboratory was performing variant testing. Simply because, if it was being done for a CLIA purpose, it would need to be done in a laboratory that met the requirements for high complexity testing. And so, I don't really know that it's even appropriate to be talking about Certificate of Waiver in this testing.

JASMINE CHAITRAM: Right. Well, thank you, Amy, for being on.

AMY ZALE: You're welcome. You're absolutely welcome.

JASMINE CHAITRAM: And we are going to move to our last speaker today, which is Tim Stenzel from the Food and Drug Administration. And Tim is also somebody that continues to join these calls and provide these updates. And we appreciate his time as well. Tim?

TIM STENZEL: Thank you, Jasmine. And I appreciate the opportunity to come on and try to help. A number of questions. Hopefully, I have enough time to get through them. I have a question regarding, I'll read it, unsupervised patient self-collection of anterior nasal or nasal mid-turbinate swab.
Can health care facilities have patients do unsupervised self-collection within the health care facility, using facility-developed unsupervised self-collection instructions? Or does unsupervised collection performed at a health care facility, require FDA specifically approved patient collection instructions, within the EUA for the test that is used, i.e., similar to home collection patient instructions?

We have distinguished this from home collection when it is performed within a health care facility. So unsupervised COVID self-collection of anterior nasal or mid-turbinate swabs, within health care facilities, do not require an FDA authorization. Do not need to be FDA-authorized.

Second question. In regard to the variants in serology tests, has it been determined if test developers need to evaluate the impact of novel variants, on the performance of antigen tests? If so, is there any recommended source? So of course, we recently issued guidance, which includes our high-level recommendations for test developers, to evaluate the impact during their development process and after authorization. Evaluate the impact of viral limitations and variance on the performance of all tests, including antigen and serology tests.

As we develop more specific recommendations and methods by which to evaluate this impact, specifically on antigen and serology tests, of course it's much easier with molecular tests, we will include those in

updates to the antigen and serology templates. The serology was just last week, updated to match the language in the recent variant guidance.

In general, we recommend searching sequence databases for mutations and variants circulating in the US. At a frequency or importance if it's an important new variant. And determine if there's any potential impact on your test. If there is a potential impact, we ask that you contact the FDA, and discuss your plans to follow-up with additional work. And we'll work with that developer. The FDA is, of course, doing their own analysis. But we, through this guidance, have asked test developers to join this effort.
Next question. What is the status on the availability of FDA-approved, or EUA antibody testing for COVID-19, with commercially available kits that can be used on serum sample testing and saliva sample testing, to determine if vaccinated individuals have developed antibody responses?

Of course, we have not authorized a saliva test yet. There are currently over 70 antibody tests, authorized for use with serum, plasma, or blood. At this time, none of these have a specific claim regarding the vaccinated individuals. And not all are useful for each vaccine.

Clinicians can use serology tests for taking care of patients. And we urge caution though, that knowledge of the specific test and vaccine is important and should be determined. We have recently heard of false negative serology results, due to the use of a test that would theoretically reveal an immune response to certain vaccines - that would theoretically not reveal or be discordant.

And for example, an N protein serology test will not detect an immune response to a spike protein, a vaccine. Which makes sense. But it's important for this information to get out there. We are looking into how we can make this information more widely known. It may be through a safety communication or other means. And of course, we do welcome submissions that examine this issue for serology tests. And if the data support whatever they're claiming, we'll authorize for that purpose.

Next question is, I remain concerned about off-label use of new rapid antigen tests for home use. Indicated only for those suspected of recent COVID-19 infection, versus for general surveillance other than the new Ellume test common. So this is getting at the fact that, the FDA has not reviewed their performance, the performance of prescription home tests in the symptomatic population.

And so there has been some recent information. And one of those bits of information was presented earlier on today's call, about the use of serial testing. So as we've previously said, including in a prior FDA frequently asked questions, and in the fact sheet we issued last week, a health care provider may order a test for screening, even though it is not authorized for screening. It is important to be aware that certain tests, including labeling, that states that the tests should only be used for symptomatic individuals. These tests should not be used for screening.

And that is a very specific call-out. That's unique to just a few tests. And it's not broadly applicable to tests. And it does not apply to any of the antigen tests. For home tests, unless the test is authorized for

screening, it generally would require a prescription from a health care provider, who can determine whether it is appropriate for that individual to use.

As noted in the new supplemental antigen template we issued last week, we will now consider an asymptomatic screening claim for serial testing, without preauthorization validation in that population. This applies to point-of-care tests, as well as home tests. So as long as in symptomatic individuals, for which we've authorized that test, performance meets at least 80% sensitivity, or PPA, with a lower bound of at least 70%. We will allow a claim update without premarket data if that test is incorporated into a serial testing plan.

And then we will post-authorization, ask for a post-market study that will confirm performance in the symptomatic population. If for some reason, the serial testing in that device is not able to show sufficient sensitivity in the symptomatic population, we would remove that additional claim.

Also for home RX tests, they're already authorized for home use, self-test, or otherwise. Well, self-test generally. They can request an update to their authorization, as long as they have met that performance expectation, in symptomatic patients in their original authorization. They can update their authorization request to be included as an over-the-counter test, as long as there's a follow-up post-market study in that population, to confirm adequate performance.

We believe that the use of serial testing, in this way, outweighs the risk of this approach. And of course, if the data comes in for any of this post-market and does not continue to support any symptomatic claim or an over-the-counter claim, we will pull back on those specific authorizations.

Next. Does the FDA have an overview of the approved intended uses for each FDA EUA-approved test? We approach this sometimes individually. But there are three broad categories of indications included in authorizations for diagnostic SARS tests. And those are antigen and molecular tests.

Suspected of COVID-19, this indication is the most common. Individuals suspected of COVID-19 by their health care provider. So this includes individuals suspected of COVID-19, may be symptomatic and are asymptomatic for other reasons, such as an exposure or areas of high spread.

The next authorization indication is for screening. We've authorized, I think, about a score of these screening claim tests now. Everything over the counter has a screening claim. Screening is an indication, typically indicates the following language. Individuals with or without symptoms, or other reasons to suspect COVID-19. So this is looking, even in low incidence population, can the test accurately detect someone who is asymptomatic?

This indication is considered a broad-based screening claim, such that the test can be used on any individual, regardless of symptoms or exposure. And finally, we have a subset. A small subset of tests, where we've called out that they only can be used on symptomatic patients.

And this is a limitation that is made only after data demonstrating that performance is lower in a certain category or situation, where we call out that limitation specifically in the test labeling. And this is typically, a rare event, fortunately, among all EUA-authorized tests.

The next question is, how will new variants affect the EUAs current tests? The FDA continues to monitor the impact of our limitations and currently authorized tests. And we'll continue to work with the EUA holder if any issues are identified. As I explained earlier, the recent guidance has asked the EUA holders to get involved in this process.

If one or the other of us, or both of us, come to the conclusion that there's an issue or potential issue, we will make that information publicly known. As we have previously done for a specific test, and that was a communication. Plus, the labeling of the test is updated with that new information.

Next question. And this is the last question. There are many of them today. What would be the pathway for SNP assays approved for surveillance of variants of SARS-CoV-2? We now routinely ask that all of our positives, in a high throughput manner, using a panel of discriminatory SNPs. We know whether an individual is infected with a variant of a concern interest, within about four days of sample collection. Sequencing is critical for identifying new variants, but it will never provide comprehensive monitoring in real-time. It is too slow, too expensive, and too low throughput. High throughput SNP technology, single nucleotide polymorphisms. It was available to assay the majority of all positives on a national scale, quickly and inexpensively. Therefore, we need guidance on getting SNP assays authorized on an emergency basis.

So I understand where this is going. There is also mutation assays, specific mutation assays of development interest out there. We have heard that and discuss that with potential sponsors. One thing of caution is different variants can have very similar mutation profiles. And so this strategy alone may not positively identify, specifically, a specific variant. It does depend on the test design itself.

And if such assays seek FDA authorization, we encourage them to come in and discuss with us the design of their assay, and how they would like to validate, and whether that test can be authorized. The FDA currently, I should explain, is not regulating purely surveillance activities during this pandemic. And we agree that monitoring of variants and mutations is very important to me and support all methods that would achieve that end.

It may also come to pass that mutation or variant detection, is important to determine if someone will respond to a specific therapy. If results will be reported to patients, as discussed in the viral mutation guidance, we currently believe that whole genome sequencing tests are best suited for genotyping, due to their ability to detect both known and emerging mutations and variants. And clearly establish the variant that's present in that patient.

However, if developers of SNP kits or mutation kits have alternative proposals, that get around some of these limitations, or are defined in a way that are safe, and/or if sound science supports therapy selection,

based on specific mutations, we encourage those developers, as I said before, to reach out to the FDA and discuss. And we will, of course, consider them for EUA review and authorization. So that ends the last question. That was given to us ahead of time. And hopefully, those answers are clear. Thank you.

JASMINE CHAITRAM: Thank you, Tim. I think we can squeeze in one question from our Q&A box. And the question is, how is the BioFire Respiratory Panel, has gone through the De Novo pathway, will it retain its point-of-care waived status? Along with moderate high complexity testing? Or will it be moderate high complexity only?

TIM STENZEL: So for the BioFire RP 2.1 EZ, it is available for use in CLIA waived or point-of-care environments. And it was not removed from the EUA list, only in the BioFire RP 2.1. Hopefully, that addresses that question.

JASMINE CHAITRAM: Great. Thank you. And maybe we can squeeze in one more. Can you explain the difference between direct-to-customer versus over-the-counter, for at home collection kits that have gotten an EUA?

TIM STENZEL: We are clearly using the language in different settings. And on the FDA authorization website, we do go into these definitions. So you can double check them there. But direct to the consumer is limited to home collection, and not home testing. And over-the-counter, we have limited that language to home testing. So that's how we distinguish those two categories.

JASMINE CHAITRAM: Thanks. And now that the BioFire has gone through De Novo pathway, are you still accepting EUAs? Submissions for EUA?

TIM STENZEL: Absolutely. There's no way that test can meet all of the molecular test needs for the country. It's a very important and useful test, obviously. But it will be a long time before full authorizations can meet the nation's needs. And even though under law, there is a pathway that we are required to go through. And we have the opportunity to end the EUAs of others. We typically haven't done that in the past. We have not, in my knowledge, done that in the past, for any open emergency that still exists. For example, Zika and-- I can't think of the one.

But any other recent and still open emergencies, that have been declared and remain open. And we have no intention of doing that this time. There's just too big of a need. We see the EUA pathway is still being important. We are still accepting prioritized molecular antigen and serology test submissions.

JASMINE CHAITRAM: Tim, thank you so much. I really appreciate you being on the call today. And we are just about at the end of our call. So I just wanted to thank all of our speakers for being with us today. And also, remind all of you to sign up for our LOCS messages, if you're not receiving them. That way, you can get emails and notifications about these calls. And we thank you for joining us. And for those of you that have stuck with us for a year, we're glad that you could be here, and continue to stay safe. Bye.