Clinical Laboratory COVID-19 Response Call August 9, 2021

Agenda

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- Use of Cycle Threshold (Ct) Values
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- SARS-CoV-2 Variants Update
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JASMINE CHAITRAM: Hi, everyone, and thank you for joining the Clinical Laboratory COVID-19 Response call. I'm Jasmine Chaitram. I'm the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems. And we've been hosting these calls since March of last year, 2020. As you can see, we've got a pretty full agenda today. And so we're just going to go ahead and get right into it after I give a few updates about some things you need to know with regards to just logistics for the call. And then also just kind of do the background intro on the Division of Laboratory Systems for anybody who is new to our call.

And with that, actually, inserted-- with the help of some other folks this time-- a couple of slides about our division so that you're clear on who we are. This division is within CDC. And as I've said before, we do a lot to support clinical and public health laboratories.

In the slide deck you'll see our vision and mission statement. In particular, we have four goal areas, and I've mentioned this a few times. We are supporting clinical public health laboratories in the area of quality and safety, workforce and training, also informatics and data by a repository of science, as well as preparedness and response. And that has led us to host these calls where we're providing information to the clinical and public health laboratory community.

We also have, now, a website that acts as a one-stop shop for you for information that we have provided to the clinical community that could be our LOCS messages. That's our Laboratory Outreach and

Communication System. We send out emails from this. You probably receive one today announcing the call. We've also sent out other emails, important information. And we've been doing that since January of last year. And all of those messages are archived on this website.

And we also have, on our website, an archive of all of these clinical laboratory calls, the transcript, the audio, the slides, everything is there. So you can always go back if you missed something, or you have to drop off early to find information about our calls. We also provide links to important information from CDC related to the COVID-19 response. And having trouble moving my slides.

OK, the next call will begin on Monday, August 23rd at 3:00 PM. We host these calls every other week, and so it's every two weeks. And as I said, next call will be two weeks, August 23rd. We usually send out the agenda the Friday before the call so you can know what to expect.

We have asked in the past, and continue to ask, for your feedback, especially in the area of training and workforce development. And those specific topics can be sent to the labtrainingneeds@cdc.gov email. And finally, how to ask a question during this webinar? We do ask that you use the Q&A button at the bottom or within your Zoom button features.

And we prefer that over the chat because then we can have a record of the questions. And if you want us to get back to you, if we're not able to get to your question during the call, it's helpful to have an email address and a name. And we can try to follow up after the call.

If we don't follow up after the call, it's usually because maybe your question was something that other people were asking and we're going to-- instead of answering your question alone-- we're going to host a topic that will be related to your question as an agenda item on a future call. We do apologize in advance for any questions that we can't answer during the call. There are quite a few of you on these calls, and it is hard to squeeze it all into the time that we have. And so we ask for your patience on that.

We also ask that any questions that you submit are related to laboratory issues. If we get questions about other subjects, especially things like vaccinations and clinical care, I mean, those are things that we don't normally have subject matter experts on these calls. And they are not able to answer. So we usually won't be able to ask those questions during the call.

We will try to get solved for you but we prefer that these questions and this call be focused on laboratory issues. And, I think, with that, just one more reminder, and that is that the slide decks that we post on our preparedness website, the archive that I mentioned, they may contain presentations materials from panelists that are not affiliated with CDC. So just a reminder that the content may not necessarily reflect CDC's official position.

And with that, we will go ahead and go into our first speaker, who's Brandi Limbago from the CDC Laboratory and Testing Task Force. And I believe she was on the last call. And we've got her back today

with us again. And we appreciate her time. She's super busy these days. And she'll be talking about the use of cycle threshold (Ct) values. Brandi?

BRANDI LIMBAGO: Thanks, Jasmine, can you hear me all right?

JASMINE CHAITRAM: I can hear you great.

BRANDI LIMBAGO: Great. Great, great. Thanks. Hi, everyone. Thanks for your attention this afternoon for joining us. Just wanted to answer or try and respond to some of the questions we've been getting in through various avenues in about the past week or so.

Recently, there was an MMWR that came out from CDC talking about an outbreak. And then, of course, with that also, it made mention of a comparison of Ct values between different populations. Notably, in this particular outbreak, it was in Massachusetts. It was between the Ct values among people who were unvaccinated compared to vaccinated people.

And we got a lot of questions as a result. The CDC is now recommending that we use Ct values. Do they need to be reported routinely? How should we report them? All of this. So I just want to take this time to say that CDC has not changed our position-- our overall position on the use of Ct values for the individual level or for individual reporting.

So there are a lot of reasons that Ct values can change. They are, of course, related to the amount of nucleic acid present in the sample. But they are not an indicator of infectiousness in the person, nor are they really even an indicator or a reliable indicator of viral load.

At the individual level, our position continues to be that the diagnostic assays that are approved for use are all qualitative, not quantitative. The answer should be positive, negative, or indeterminate. But there might be utility for large epidemiologic studies or comparisons at population levels or for surveillance purposes.

And as I said, maybe comparing vaccinated or unvaccinated people or people who might have a connection with one kind of strain or another. And there might be some utility there as an indicator, but always in conjunction with other epidemiologic logic data. So that's really all I wanted to say. And we will be updating our cues online. So all of this will be there for you to go and reference soon.

And with that, I can take any questions or whenever we were taking them. Jasmine, and I forget if we're supposed to take them now or at the end.

JASMINE CHAITRAM: Thanks so much, Brandi. We usually take them right after the speaker gives the update. I don't see any questions for you at the moment. I forgot to mention that we didn't have any slides for your portion of the agenda here, so just kind of putting that out there.

OK, so here is one question that just came through. It says, how should labs handle situations where states mandate CT value reporting on the patient level?

BRANDI LIMBAGO: So this is a hard one. I don't exactly know how to advise any given clinician or reporting laboratory where a state mandate might conflict with FDA reauthorization or the instructions for use for a given assay. I do think that is a really hard situation.

I guess I would say that if you're able to report them and they are reported for public health purposes, I think that that is within what CMS will allow. I certainly can't say exactly how that might be reported on an individual report. And I would encourage folks to always try and make sure that these are going to public health as opposed to clinicians because that is where we know they will have utility.

JASMINE CHAITRAM: Thank you, Brandi. That was a tough question. Somebody is asking about a recording of the call. And as I mentioned at the beginning when we opened up that we have this preparedness portal that has the archive of all these calls. It does include the slides, the transcript and the audio from all of these calls. So that will be posted. It usually takes us about a week to get it up on the website, so look for it in about a week from now.
I'm not seeing any other questions, Brandi. And I know you've got lots to do, so thank you so much for joining us today.

BRANDI LIMBAGO: Thanks for having me. Bye.

JASMINE CHAITRAM: OK. So we will now move to our next speaker. I don't know why my slides don't like me today. Hang on one second. All right, here we go. All right, so our next speaker is also from the CDC Laboratory and Testing Task Force. And she has been with us before. Jessica Chen is going to give us an update on national SARS-CoV-2 surveillance as it relates to variance. Jessica?

JESSICA CHEN: Thanks, Jasmine, for that introduction. And good afternoon, everyone. Thanks for joining us today. Today, I'm just going to highlight some data from our genomic surveillance efforts. Next slide, please.

First, I'd like to mention that all the figure is an estimate but I'm going to show today can be found on the variant proportion page on the COVID data tracker. And we'll be sure to put a link in the chat for you so that you can access that website.

First, I'm going to present our national Nowcast estimates of SARS-CoV-2 lineages in the United States. These now cast estimates are projections intended to provide more timely information, while accounting for the limited sequence data availability as we collect more sequence data from this time period.

These data that I'm showing today are from a two-week period ending July 31st. Starting last week, we are now displaying the three deltas of lineages AY.1, AY.2, and AY.3 separately from the DL1.617.2 parent lineage. But you should know that these are all still considered part of the Delta variant of concern.

Delta, an aggregate, so these three separate lineages as well as the parent lineage has increased from 82% to 93% in this time period. Most of the US sequences which our delta are still that be that B.1.617.2 parent lineage at 83%. But notably, AY.3 makes up 9%. AY.2 and AY.1 make up lower percentages at 0.8% and 0.1%, respectively. B117 or alpha on the other hand continues to decrease over this time period from 9% to 3%. And P1 or gamma continues to decrease from 4% to 1%. Next slide.

This figure shows our regional Nowcast estimates of lineages. B1617.2 or delta is predominating in all HHS regions. And aggregating across all these delta sub lineages as well as the parent lineage, we find that delta is highest in region 7 and 8.

Well, accounting for about 98% of sequences in both regions. The sublinear JY3, specifically, is highest in region 7 and AY.2 is highest in region 9. We also are finding that B117 is decreasing in all regions, and is at less than 7% in each region. And gamma pr P1 is also decreasing in all of these HHs regions with less than 3% in each region.

And that concludes my update. I'd be happy to take any questions you may have.

JASMINE CHAITRAM: Thanks so much, Jessica. We did get a few questions. Several of them are around lambda variant. And can you comment on that one? And if CDC is monitoring, and if CDC is seeing an increase in incidents.

JESSICA CHEN: So lambda is also called variant C37. We've been monitoring this very closely over the past few months. We have not seen lambda increase in incidents. At its highest level, it made up half a percent of our sequences and has continued to decline since that time.

JASMINE CHAITRAM: Great. Thank you so much for answering that. Is there any clinical relevance in distinguishing AY.1, AY.2 and AY.3?

JESSICA CHEN: Yes. So AY.1 and AY.2, you may have heard these in the media referred to as delta plus. This is not an official CDC classification or a WHO classification. That's just how people are referring to them.

AY.1 and AY.2 have a mutation that's been associated with decreased effectiveness of a certain monoclonal antibody treatment. However, AY.3 is more similar to the parent lineage, and it doesn't have that particular mutation.

JASMINE CHAITRAM: All right, thank you. How many samples are these variant proportion estimates based on?

JESSICA CHEN: Sure. Let me quick see if I can pull up those numbers. I know that by the time we finish, I think-- I know for the two-week period ending July 17, we had close to 24,000 sequences. So it may be

a little bit less than that since we're still collecting data for the time period. But yeah, I think I'll have to get back to you on that.
But yeah, that's something we're tracking closely. And I think we're-- the last time we calculated the percent of clinical cases that we were sequencing, we were right about 8%. So I hope that that information helps.

JASMINE CHAITRAM: Thank you. OK. Are you able to comment on the primary mechanism behind the increased transmissibility of the Delta variant?

JESSICA CHEN: I can't comment on that at the time, but I can get back to you.

JASMINE CHAITRAM: OK. And can you talk about what is the approximate time lag from taking a patient sample to when CDC might provide results? And it's not specific here on what we're talking about, but I'm assuming we're talking about the sequencing of variants because of the topic.

JESSICA CHEN: Yeah. Generally about two to three weeks that includes the time that it takes for the sample to get to us, for the sequencing to be performed and the analysis to be performed for a sequence to make its way into a public repository.

JASMINE CHAITRAM: OK. I'm going to ask you one more question before we move to our next speaker. Are there any differences in proportion of variants in infections in vaccinated and unvaccinated?

JESSICA CHEN: I haven't seen our data broken out like that. However, the vast majority of sequences right now are delta, so I would anticipate that delta is the predominant variant that you are going to see in most cases regardless of vaccination status. And this doesn't have to necessarily do with delta. Its ability to infect people who are vaccinated versus unvaccinated, it just happens to be what's circulating at a very high level in the US right now.

JASMINE CHAITRAM: And then, there is a question that's been posted a couple of times about can we use mutation specific PCR for the reporting of patient mutations. And I don't know what your thoughts are on this, Jessica, but it's my understanding that there are no FDA authorized for diagnostic testing PCR tests that detect variants at this time.

So if there's no diagnostic test for that purpose, then we wouldn't be reporting those patient results for diagnostic purposes. But I'm interested in your thoughts.

JESSICA CHEN: Yeah, that's my understanding as well. We are heavily reliant on sequencing for understanding the variant information. And then it'd have to be a specific test that's designed for that patient reporting even in that case. So yeah, I'm not aware of any tests either.

JASMINE CHAITRAM: I agree. And we don't have FDA on the call this week to help answer that question. But we will follow up with them. OK. So thank you so much, Jessica. I think I'm going to move to

our next speaker just so that we have enough time to get through all of our topics today because we have two more presentations. Thank you for joining us, again, and we appreciate all the information that you shared.

So our next speaker is Bruce Stromberg from the National Institutes of Health-- NIH-- and he will be talking about the RADx program-- the Rapid Acceleration of Diagnostics Technology. Bruce?

BRUCE STROMBERG: OK, thank you, Jasmine. And Thanks to Wren and to Bill for inviting me to come and give this talk. So you can see on this first slide a picture of some over-the-counter tests that are available in pharmacies. One of them happens to have quantum dots in them. That's the illum test. So I kind of am surprised that we have quantum dots on the shelves in medical devices. And this is really a talk a bit about that story how that came to be.

I'm from the NIBIB. That's one of 27 institutes and centers at the NIH. Our Institute is focused on engineering and technology. So I'll talk about RADx the program that we've launched to try to accelerate this process. Next slide, please.

We started with a congressional appropriation. So in April last year, this was actually quite unexpected. There was 1 and 1/2 billion appropriated to NIH. 500 million went to NIBIB, which is really quite a lot for us as a relatively small institute. And we launched this program-- Rapid Acceleration of Diagnostics-- in collaboration with the Office the Director, so very close interaction with leadership at the NIH to expand COVID testing technologies, the number, the type, the access, optimize their performance both technologic as well as operational, and match community needs.

The NIBIB leads the technology development portion of this. This includes making new technologies, innovation to do entirely new things, as well as scaling up existing technologies in innovative new ways. There are two additional flavors to RADx.

There's RADx-rad, which is very forward-looking technologies. A continued investment in them over several years. And the next RADxUP for underserved and underrepresented populations. That's its own dedicated $500 million program that's had two phases of awards and is having very significant impact on academic centers around the country.

We've partnered, of course, across the government immediately with BARDA. And there's a real financial input from BARDA, over $300 million, into the program. The Assistant Secretary of Health in the Testing Diagnostics Working Group, the FDA, DoD, the White House Pandemic Testing Board, and of course the CDC. So this has been an all government-initiated effort. And next slide.

And the platform, really, the operational platform underneath it all is an existing NIBIB network for those of you who are familiar with NIH funding. It's a U54 cooperative agreement. It's called POCTRN-- Point of Care Technology Research Network. Multiple institutes that have actually invested in this network that

we've established over the years, going back to 2007, we expanded it quite dramatically in order to take on this particular problem.

So there are more than 900 experts and current contributors from government, academia, industry, not for profits. And we've added, into the network, some unique structures. A validation core, which is at Emory Georgia Tech. Wilbur Lam leads that core, and he is actually going to follow me in the presentation.

They validate independently all the technologies that are proposed and worked on in the network. A clinical studies core at UMass led by Dave McMannis and Laura Gibson. Standardized trial design, they have a digital health platform a single IRB for studies.

And a deployment core, which is centered at CIMIT, the Innovation Institute at MGH, which deals with supply chain, user community, when to test out work. I recommend everyone take a look at that. That summarizes a variety of testing approaches, it's connected with the shoe testing common as well as project N95.

So the academic institutions that I mentioned are Emory, Georgia Tech, Johns Hopkins, UMass, Northwestern, CIMIT at MGH is the main coordinating center. And we've added not for profits in this to help us expedite, review and funding of ideas, testing and validating of every concept that comes through it, and provide expert guidance for every team. Next slide.

And the teams are optimized and selected through a process that we call an innovation funnel. We've reduced this practice at a really quite a spectacular scale. We opened the funnel on April 29th of 2020. And there were about 3,000 applications started. It was really a call out to the innovation and entrepreneurial community where we had enormous response.

716 eventually completed applications, and they went through 140 deep dives or Shark Tank reviews of each of the projects where every project concept gets teamed up with an entire separate team that spans a whole bunch of domains of expertise from technology to manufacturing and commercialization. We funded 47 phase one projects which were on a real fast track, typically about a million to perform and meet milestones in a one to two-month period.

And then we ended up funding 33 projects in phase 2 which is manufacturing scale up. Throughout this process, there's de-risking, working with regulatory. So the FDA has been a critical partner throughout all of this. And by the time you make it through the funnel, in principle, you have emergency use authorization, and you're scaling up manufacturing. And we've compressed what is typically a five-- or six-year process into five to six months. We spent about $600 million in phase two awards. Next slide, please. And here is kind of a snapshot of a few of these. They span point of care and home technologies, both RT-PCR as well as antigen assays-- antigen, including lateral flow assays. Of course, they're the dominant ones. But also, new types of approaches, like waveguide sensors made by, for example, Qorvo, in this particular case.

A couple of these are fully over the counter and home-approved. They're laboratory approaches that are supported, both new technology, such as the Quanterix single-molecule detection assay, which is a laboratory-based approach that potentially can do quantitative measures of viral load by looking at viremia, a really nice and innovative and sensitive platform. You may be familiar with the Fluidigm platform, as well as another one that potentially can do surveillance with variants, which is being developed by PathogenDx.

Most notably, PathogenDx and Fluidigm are both working on interesting approaches for surveillance that are non-NGS-based approaches. We've also supported laboratories like Broad Institute, Helix-- they're very active-- Aegis, PathGroup, Sonic Healthcare, and so forth-- and lab products, including CRISPR, products from Mammoth Biosciences, serious nanoscientists, which makes a nanoparticle preconcentrator, which improves limits of detection by up to an order of magnitude. Saliva collection approaches. New swabs. Next slide.

The upshot of all of this is, five months after launch, we were able to already start to make a dent in increasing capacity. Roughly 20 million new tests were added in September 2020. And if we look at the cumulative capacity through June of '21, it's over 500 million new tests that we've added. We're, in June, at roughly 4 million tests and test products per day. 27 EUAs have been authorized or issued for these approaches, including the first OTC, EUA.

More than 100 companies have actually been supported. It's not just the ones that make it to phase two. But there are many with promising ideas that we've managed to redirect and support in other ways. We've spent a little over a billion in special congressional authorizations. And there's been well over $1 billion also raised in private capital to support all these companies that are expanding.

In addition to making the tests, we've also gotten involved in partnerships, most notably with CDC and the RADx community, to look and see how we can do over-the-counter testing in people's homes, how effectively people can take this up for a screening and cadence-based testing multiple times per week. We have three sites that are ongoing. One's in Pitt County, North Carolina, another is in Hamilton County, Tennessee, and the third one is in Washtenaw County, Michigan. These are both efficacy and effectiveness studies with various outcome measures and an optional app, which partners with Amazon for ordering tests, providing reminders and instructions, also reporting results-- in Michigan and Tennessee in particular. Next slide.

And on that topic, simultaneously, we've been working with a variety of collaborators to build digital health tools. And one of them is care evolution, which has built an app that provides instructions for use, has symptom surveys, can provide the capacity to read, for example, lateral flow assays. And working with the Office of the National Coordinator, NATHL, we've identified some common data elements from these at-home tests. And so it is now possible-- there is an existing pathway-- for people to take tests at home and push them out to ATHL, which can send them to both state and federal databases. This is still obviously a

work in progress, but much needed considering the volume of point of care and home tests that we're not capturing in the country. Next slide.

We've also, in January-- some of you may remember the FDA guidance on a mutation communication, basically, that is a concern about the performance of tests for different variants. In January, we launched a variant task force which cuts across our RADx team, in particular, the validation core, colleagues at the University of Washington. At the center of it is an informatics database that we've supported from a company called ROSALIND.

And the goals are to look at the impact of variants on test performance, both nucleic acid and antigen tests, which can be done using computational approaches with ROSALINED looking at primers and epitopes, calling up information on GISAID and GenBank, and doing calculations, basically, of the potential impact.

And then through our federal agency collaborations and work with colleagues in the field, developing a biobank and standard protocols for variants, testing them at the Atlanta center-- that's the Emory Georgia Tech Center, doing wet testing as well and working with manufacturers. This is a whole network for assessing the performance. We also are looking at potential ways to leverage all of this work in order to design tests, effectively SNP chips type of approaches, for variant surveillance that would not be NGS. Next slide, please.

What about future directions? Well, there's clearly a performance gap in between antigen tests and PCR tests. We do now have point of care handheld PCR. Certainly, there's lab PCR. We'd like to have tests that perform as well as laboratory PCR but are as inexpensive and easy to deploy as antigen tests. Next slide, please.

Here, there's an enormous amount of work going on and new technology, from microfluidics and nanomaterials. About 16% of all of our applications have been in advanced nanosciences-- single-molecule detection approaches, integrated circuits, waveguides and photonics-- those are sort of the brute force approaches. But also, thinking cleverly about how we can leverage existing technologies with new guidance and FDA authorizations.

Working collaboratively with FDA, we've helped, through studies at the University of Illinois and UMass and Johns Hopkins, ways to think about doing multiple lateral flow assays every two to three days. They can have effectively the same sensitivity as RT-PCR by capturing the growth, the ascendance, of the viral load, if you do your interval on cadence screening in just the right way. Also, pooling point of care RT-PCR, which is quite convenient.

But standardized techniques need to be done if you're going to deploy those handheld PCR devices, for example, in a classroom. But it's been shown. And Wilbur's team is also leading this effort, that you can pool up to 10 people-- possibly even 15 in a classroom, in a home-- with very fast turnaround times. And again, the validation core at Emory is also looking at pediatric self-swabbing, working in collaboration with

FDA, to help optimize workflow in home and schools, showing that children can do this as effectively as a health care provider. Next slide.

To just summarize, RADx has been a program that's really an entirely new process, with many different stakeholders working collaboratively to accelerate this whole cycle of design, build, test, deploy, and manufacture, and to have impact. We've leveraged an existing network, with added capabilities and connected partners together, across the government. We note that-- and of course, all of us recognize that technology needs seem to change from week to week and month to month. We're having, of course, increased vaccination and increased variance.

What does that mean? Well, we continue to need more sensitive and accessible over-the-counter point-of-care tests. We obviously, as we approach fall, need to be able to multiplex with other pathogens and expand our digital health and reporting networks. And rapid variant assessment, which was referred to just a few minutes ago on the call, that does not involve next-gen sequencing-- with some layered surveillance approaches, like in bioinformatics-- could be promising approaches for the future.
We would like to leverage RADx processes and technologies for other pathogens and preparedness as we look to the future. And we reopened the innovation funnel temporarily. In three weeks, we had another 100 applications. And 34 of these are in the Shark Tank deep dive. We hope to make some awards in these areas, meeting those needs in the coming months. Thanks very much.

JASMINE CHAITRAM: OK. Thank you very much, Bruce. That was a great overview of the RADx program. And there are a few questions. And the first one says, we are seeing use of BinaxNOW as a point-of-care test performed by nursing pharmacy or occupational health to monitor employees for breakthrough infection. Is this practice founded in data from studies? And I'll just add to that, to be more specific to RADx, the question could be, is RADx funding any specific studies around using these point-of-care tests to monitor individuals for breakthrough infections?

BRUCE STROMBERG: Yes. It's a tricky question, because with breakthrough infections, initially, we weren't sure whether the antigen tests would have sufficient sensitivity, since they are challenged in terms of their limits of detection. But for the Delta variant, we're seeing that viral loads can be quite high. I don't know of any systematic studies that are designed to look at that, although perhaps the CDC may be aware anecdotally.

We have been seeing, in HHS databases, a number of breakthrough infections reported in studies that HHS overall is doing. And as we analyze the data from Washtenaw County, Michigan, and Tennessee, and North Carolina, one of the problems with that data is that we're giving it to people to do in their homes-- the tests. And we're not getting full reporting. It's really hard for us to assess that. Perhaps the CDC can address sort of their knowledge-- your knowledge-- on what's going on in point-of-care tests that are reporting.

JASMINE CHAITRAM: Thanks. We'll have to follow up on that one. Another question was about the concerns around diagnostic error generated from point-of-care tests, and is RADx doing anything to fund or investigate QC or quality assurance issues?

BRUCE STROMBERG: Sure. When the tests are used on-label in symptomatic individuals, regardless of vaccination status-- I should throw that in there-- their performance is typically quite good, generally better than 90% sensitivity and 95% specificity. Of course, it will depend on prevalence and pretest probability. Those are things to consider in deploying those tests, a hedge against that. Most of the manufacturers, like Binax and Quidel, are selling packets of two. And this moves into the screening authorization, which recommends testing twice, roughly, in a week.

And that mitigates against the possibility of an error in your test the first time around. That, combined with recommendations to reflex testing following CDC guidance, I think are really good ways to approach this. We are also trying to push forward new technologies that are having better limits of detection so we don't have to worry about having to have multiple tests in a week like we do with the antigen assays. And this is possible. This generation of technologies are really emerging right now.

JASMINE CHAITRAM: Thank you. Another question. Can you comment about the true public health self, at home, over-the-encounter antigen rapid tests that actually serve the underserved, and empower the public to test and isolate themselves quickly? Binax is great if you have a smartphone network and actually have $8 to $25 to spend.

BRUCE STROMBERG: Well, in all of our-- actually, $8 is not too bad for tests, although it can be lower. And certainly, the cost of goods suggests that it should be lower. In all of our surveys that we're doing in these communities, we're finding that, in general, underserved communities are heavily targeted in these efforts. And there has been, really, substantial uptake and enthusiasm for tests in those communities. Whether they're reporting them or not is another issue. But we've been able to distribute more than a million tests with a tremendous community response.

We have community organizers that are also distributing these, in addition to being able to order them online. What we, then, do rely on is personal decision-making at this point, when they do get positive tests. But I think, from a national perspective, we probably need to coordinate a little bit better to provide reimbursement and some additional incentives for people, when they do get positive tests, to make decisions to stay home from work or from school and to act on them. It is a very complicated-- many features are woven together with this.

JASMINE CHAITRAM: I agree. And one of the things I'm seeing a pattern in some of the questions that we're receiving is about reporting for those at-home tests. And you touched on it a little bit and the answer you just gave. And what I would add is that there are efforts, in the US government, to help test manufacturers that are creating at-home tests to develop or a partner with software companies that can create mobile apps to facilitate reporting.

And of course, the tests that involve a health care provider to interpret the results also facilitates reporting in the sense that we hope that the health care provider is reporting those results to the health department. But to answer some of those questions about reporting, and how are we ensuring reporting, I think it's a very difficult thing. Because there isn't a way for the US government to mandate that individuals that buy an over-the-counter tests report to public health-- at least not at this time. So that is a challenge.

BRUCE STROMBERG: Yeah. I mean, that in and of itself is kind of its own topic of conversation. But there are ways to further incentivize that. And we're seeing enormous response, just in Washtenaw County, Michigan. Even with the high vaccination rates in Ann Arbor-- the sort of companion city as Ypsilanti, which has lower vaccination rates-- we've seen about 350,000 tests taken up by the community in roughly a month. It's been very gratifying to see the response.

JASMINE CHAITRAM: Right. I did have another question for you. Somebody asked about, how would they submit an application to RADx if they had something that they thought was worth exploring?

BRUCE STROMBERG: Well, at this point, the applications are closed. The funnel has closed. We've had two funnel openings that have had overwhelming response. And that would far exceed our ability to support applications. We're hopeful that we'll be able to continue to do this in the coming year, and perhaps longer, as we pivot from conquering, hopefully, the pandemic-to-pandemic preparedness for the future, and we think about how to get tests more widely accessible and new technologies.
But at this point, it's not possible to apply for new funding. But working with the POCTRN network, it is possible to work collaboratively, perhaps in technology development. So I encourage everyone to look at poctrn.org. They have special calls that come up every once in a while for technologies. And that may be an entry point, as well.

JASMINE CHAITRAM: Great. Your first line mentioned the quantum dot. And a lot of us don't know, including me, what that means. And somebody asks, what is a quantum dot?

BRUCE STROMBERG: Well, they're nanoparticles that, when you shine light on them, they emit light of a different color. And unlike molecules that fluoresce, they don't bleach. The color is stable. And it's very efficient. If I send in, let's say, 1 milliwatt of optical power, I will get a very high conversion of that optical power into another wavelength altogether. And it's just a steady and bright conversion. They found their way into consumer electronic devices, like displays. They're very powerful in electronic devices.
But they have been hypothesized as very good labels or sensors for molecular imaging in small animal models-- potentially in humans. And now we're seeing them in vitro diagnostics. They are one of many nanoscience nanoparticles-- from nanopores, to nanowires, to carbon nanotubes, to nanostructured dendrimers, that we're seeing in applications. These kinds of things have been in laboratories around the country, around the world, since the nanosciences initiative in the United States from around 15 to 20 years ago.

But we have never seen them at scale. There are over 100 million nanoscience products for diagnostics that were not on the shelves or available commercially that have now been sold. That gives you a sense

for the transformative power of events like this. And from our side, the engineering side, we're hoping that we'll be able to leverage those advances into many other areas in diagnostics.

JASMINE CHAITRAM: Really cool. Thank you for explaining that. We have a ton of questions, still, in the Q&A feature, but I've got to move to our next speaker to give our folks from Emory a chance to present their information as well. If you're willing and interested, Bruce, there's still questions in the Q&A that you're welcome to answer live by typing in a response. And others will see your response while you're typing it in. That's your call. But thank you so much for joining us this afternoon.

BRUCE STROMBERG: Thank you.

JASMINE CHAITRAM: We will move to our last presentation for the day. And I'm actually just going to introduce Wilbur Lam from Emory University. And he's got a team with him that, he will take care of the introductions there. And this is related to the RADx efforts. And you'll hear more about that in just a second. Wilbur?

WILBUR LAM: Thank you, Jasmine. And thank you to you and your CDC colleagues for having us. And thank you to Bruce for giving us an introduction, basically. What we have been asked to present is a paper we recently published. Joining me are Dr. Frediani, Dr. Levy, Dr. Rao, Dr. Bassett, who are all part of our team and will describe this particular project, which is a good example of what we've been doing within RADx. Next slide, please.

As Bruce mentioned himself, we're part of the POCTRN network. And this was established before COVID-19. There are several centers within POCTRN. And we, down here in Atlanta, are the Atlanta Center for Microsystems Engineered Point-of-Care Technologies, ACME POCT. Everything that we've been doing before the pandemic was really about assessing and helping technologies that are microsystems-based-- microfluidics, anything microchip-enabled-- really moving forward in the translational pathway. But push one button, Jasmine?

But as you know, this thing came about. And I don't know about you all, but any time I see a red ball these days, I kind of get a little bit of a shiver. When the pandemic started-- next slide, please-- under the direction of Bruce and his colleagues themselves, we pivoted. We served as RADx's-- and are serving as RADx's test verification center. Our charge has been to test the tests. We set up multiple infrastructures at Emory University Children's Healthcare of Atlanta and Georgia Tech in which we have different ways to assess tests.

Our virologists, including Dr. Rao, who will be speaking to you in a bit-- our clinical team, including Dr. Levy and Dr. Frediani, who's been collecting, prospectively, patient samples, and our pathology group, who've been biobanking. In addition to that, we even have a staff at Georgia Tech that does a lot of engineering assessment and usability testing. It's a multipronged approach of how to assess a test. Next slide. With that, I'll turn it over to my colleagues.

JENNIFER FREDIANI: Thank you, Wilbur. What we decided to do-- and as you are all aware, rapidly diagnosing these highly transmittable variants of concern is really going to prevent the spread of a variant of concern. What we did was, we fully verified the Abbott BinaxNOW antigen test. This is a qualitative SARS-CoV-2 diagnostic assay that detects the viral nucleocapsid protein from anterior nare swabs. And this was actually the first LFA to receive the emergency use authorization for the home setting. Here, we summarize an assessment of the BinaxNOW test in the context of its ability to detect VOCs, but also in self-administration. Anu is going to talk about all of the variant work she's done.

ANURADHA RAO: Right. As part of our multidisciplinary approach to testing the tests, we examined the ability of BinaxNOW to detect live SARS-CoV-2. And this testing-- this in vitro testing using live SARS-CoV-2 was done in the BSL-3 labs at Emory University. Next slide.

Data shown here depicts the LOD from four different wild type isolates. In the lab, we thaw the virus stock. And soon, we dilute this in a pooled negative human nasal matrix. And each of these solutions, 20 microliters of data spotted on the swab. And we follow the IFU for BinaxNOW exactly as described in the sheet that comes with the kit.

The table on the left and the graph on the right shows that the LOD of BinaxNOW varied from 750 to 9040 CID 50 for a swab, depending upon the isolate. Next slide.

Again, this is, of course, a slide from the CDC. And it depicts the estimated proportions of SARS-CoV-2 lineages currently in the population. And it's clear here that the Delta variant is the predominant variant in the population now. And it's so crucial for not just BinaxNOW, but any test, to be able to pick up variants very effectively. While we tested the ability of BinaxNOW in the lab with wild type virus, we also wanted to find out if it picks up several of the variants that are in circulation right now. Next slide.

In order to do this, Emily is part of the NIH RADx Variant Task Force program. And we have a large biobank of remnant SARS-CoV-2 clinical samples, which we abbreviate as RCS. The sequence and the lineage of each of the samples is well known to us. Using these RCS, we create panels. And then we use these panels to examine the ability of various diagnostic tests to accurately detect the other circulating variants.

The next slide shows a brief description of sample pooling, panel creation, and how we test the tests using RCS. For example, we take 8 to 10 remnant human clinical samples. Again, the sequence of this is known. The lineage is known. And the amino acid sequences of these samples that we pool match in the end protein region. So we make a pool, we mix it really well, and make aliquot-- so if you freeze at minus 80. At the time of testing, we thaw single aliquot, a diluted in the preferred matrix for a particular test.

In this case, it would be a pooled human negative nasal matrix. Each dilution is then-- RNA is isolated from each solution. And we do an internal QC for N2, which we use as a surrogate for determining viral load. We do this for all of the different VOCs we are interested in testing. And we create a blinded panel. At the time of testing, we thaw the tubes and test. In this case, it was testing with BinaxNOW. Each tube

is tested in triplicate. And after testing is completed, we unblind. We unblind the results and interpret the data.

The next slide shows the results from testing using BinaxNOW, where we tested all of these different variants. B1.2. It is non-VOC, but it is also a random clinical sample. And since it's a non-VOC but treated in the same way as the remainder, we use it as our control. And if you see, from all of the green bars, all of the different variances detected equivalent to B1.2 using BinaxNOW. We tested two different pools, pool A and pool B, of the Delta variant, which are slightly different in the end protein mutations.
And if you look at the table on the right, you can see the CTs up to which the test showed as positive. And we consider anything within three CT compared to B1.2 as equivalent sensitivity. The conclusion from our variant testing was that all VOC pools are detected with equivalent sensitivity when compared to B1.2.
Now, I'll turn over the rest of the presentation for the clinical assessment to Dr. Levy.

JOSHUA LEVY: Thank you, Anu. Thank you all for the opportunity. As Anu just nicely presented, those are our findings in the laboratory. But what about in the wild? To assess the usability and the accuracy of the BinaxNOW test amongst a clinically relevant cohort of participants, we enrolled 309 consecutive participants from our RADx testing centers. This was done throughout the greater Atlanta area from November of 20 2020 through January this year. Our criteria for inclusion were the same as the IRT criteria for the BinaxNOW test itself. And this included an age of greater than or equal to 7 years with symptoms fewer than seven days.

It's notable to mention that this does not include asymptomatic patients. A standard of care nasopharyngeal RT-PCR was utilized as a comparator. And this had to be collected within 24 hours of subject enrollment. Now, the system that was used is consistent with the standard of care at each testing center. And for this study, that includes either the cobas 6800, the Abbott Alinity, or the Panther Fusion. And then finally, we'll present the results of the structure of usability assessment reporting the device utilization and use from the patient's perspective. Can we go to the next slide?

The first figure here presents the concordance of antigen assays versus the standard of care RT-PCR. In the top right, you see a summary of sensitivity and specificity for BinaxNOW, again, across all enrolled participants. We have a sensitivity of 74% and a specificity of 99%. And as you look along the x-axis of this bar chart, we see the three figures correlate with three separate LFAs that are currently on market, either the BD, Sofia, or BinaxNOW. And we do not see significant differences between the three. However, for all three, as we go to increasing CT scores, we do see a likewise decrease and positive agreement between the LFA and the standard of care RT-PCR. Go to the next slide?

Now, looking a little bit closer, this figure shows just BinaxNOW results. In the two comparison groups, the blue bars are the adult staff-- so health care provider taking the test or collecting the sample and running the assay itself. And then in red are adult self-collected, so when the subject, a non-medically trained patient, is collecting and completing the assay. And we see, similar to the prior figure, no significant difference between the groups here-- medical staff versus patients. But we do see a decrease in performance with increasing CT levels. Go to the next slide?

And then, finally, this shows the independent use of valuation for BinaxNOW. On the bottom right-hand side, we see the groups of patients that were included in this-- caregivers, adolescents, and adults-- and just below that, we see the pooled sensitivity and specificity with patient-collected samples and we do see a decrease in sensitivity here to 57% with a maintained specificity of 100%. Now, on the left-hand side of these horizontal bars, we see responses to three questions.

And for each one, it is divided into an answer for self-collected sample, which is the anterior nare swab, and a self-administered test, which is the actual completion of the LFA. And the three questions, which we do see a high rate of confidence-- but certainly some variability within our cohorts-- are, how confident are you that you conducted the test the way it's meant to be conducted? How would you rate the ease of use for conducting the test? And how likely do you think your friends and family would be able to successfully conduct this test?

Now, when we look at the next slide, this is the summary of the use assessment for the BinaxNOW. You can see on a scale from 1 to 9, with 1 being the most efficient and error-proof-- so unlikely to cause error. This test, with a structured usability assessment, received a score of 2 out of 9. And I would encourage everyone here who's interested in the usability aspect of the study to actually look at the supplemental material. There is a very rigorous published report that we included that gets down into, really, the nitty-gritty of how to evaluate these tests in terms of usability. And with that, I will hand it off to Jennifer to wrap up the conclusions.

JENNIFER FREDIANI: To conclude, what we've learned is that, overall, antigen tests have lower sensitivities compared to RT-PCR, especially with these increasing CT values, and that sensitivity may decrease even more due to user error once these tests are moved into the home. But overall, the BinaxNOW accurately detected all of the new viral variants of concern. And overall, we feel it's a good test and a good option-- and it was mentioned before-- with the underserved populations. If we can get to the price point where there it's available to them, I think it's a good way to get them testing, and to know their status, and know when to isolate. We have a next slide with some acknowledgments. But thank you very much for your time.

JASMINE CHAITRAM: Thank all of you for joining us. We are out of time. We did not get any questions after your presentation. That was a great presentation, by the way. And I the paper was published, so individuals that want to know more can go and read that. We did get some questions about the Binax test and use on asymptomatic individuals, but you guys did mention that that was not something you looked at, so I'm not going to put those questions out there for you.

But I do appreciate you participating in our call. And that was very good information for all of us. And since we're at the end of our hour here, I'm just going to close out by thanking everybody for joining us, thanking all of our speakers today for great presentations. And I also want to thank all of our participants for submitting some really good and tough questions that we will try to follow up on, or maybe have some

future topics to address some of those that we were not able to answer. And with that, I'd like to say goodbye, and stay safe.