Agenda
Clinical Laboratory COVID-19 Response Call
Monday, January 10, 2022 at 3:00 PM ET

- **Welcome**
  - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **Evaluation of a SARS-CoV-2 Antigen Test in a Community Setting**
  - Jessica Prince-Guerra, CDC Division of Viral Diseases (DVD)
- **The TRUU-Lab Names Initiative: Towards Standardization, Interoperability, and Understanding**
  - Ila Singh, Texas Children's Hospital
- **SARS-CoV-2 Variants Update**
  - Natalie Thornburg, CDC Laboratory and Testing Task Force for the COVID-19 Response
- **FDA Update**
  - Tim Stenzel, US Food and Drug Administration (FDA)

JASMINE CHAITRAM: Hello, everyone, and thank you for joining the Clinical Laboratory COVID-19 Response Call, our first call for January 2022. We're glad that you could be here with us. As you can see, we've got a number of topics on the agenda today. I will do my normal welcoming remarks and a couple of announcements, and then we will go to our first speaker. So first, a reminder that I want to share with you is that the Division of Laboratory Systems hosts these calls. We have been hosting these calls since March 2020.

I am the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems, and our goal is to help clinical and public health laboratories everywhere in a number of topic areas including quality and safety, workforce development and training, testable laboratory data-- and that's through informatics solutions and data science projects-- and also in the area of prepared laboratories and emergency response.

And we've been serving in this role for preparedness and response now specifically for the COVID-19 response, serving as a liaison to the CDC Emergency Operation Center and the response that is led out of the Emergency Operation Center. Some other things that we have in place, related to the COVID-19 response is a Preparedness Portal. This is a one-stop shop for a lot of information that we have related to the COVID-19 response, it includes links to other CDC web pages for COVID-19.

It also includes the transcripts, recordings, and slides from previous CLCR calls. That's the Clinical Laboratory COVID-19 Response Calls. In case you missed something, you can always check here. Please give us a couple of weeks to post this information. It does take us a little time to update everything and make sure that it's accurate and ready to go on to the website. We also have our LOCS messages archived here, that's the Laboratory Outreach Communication System.

All of you who are listening to this call right now should be subscribers to our LOCS emails. If you're not, then you can send us an email at locs@cdc.gov and we can get you signed up. There's other links to other preparedness information that DLS is involved in as well on that page.

One quick announcement that I wanted to make today is about data reporting. And it's been a while since we've talked about data reporting. We have a web page that was posted in 2020 and has since been updated and we're continuing to look at reporting requirements and revise as necessary, and working through that internally and with our partners at HHS. The one announcement I want to make, today is a reminder that the “ask on order entry” (AOE) questions are optional. We've heard from laboratories that there's a tremendous burden, especially with the increase in testing demand, to enter all the information for some of the samples.

And we understand that recognize that challenge and just want to remind you that some of the questions are optional. And so if you have that option to skip a question to increase the speed at which you're accessing samples and providing information or reporting the information, we support you in that. However, there are some core data elements that are important and that are required. Things like date of birth, patient address, ethnicity, and race information is required. And we just want to remind you that those things are required.

It does help with contact tracing for the state health departments. It also helps with duplication of data because we know that individuals are getting more than one test. We want to have the best information we can about cases and the amount of testing that's going on. So just a reminder to think about that and figure out which questions are required, and which ones are optional to ease the burden of entering information.

Our next clinical lab call will be on Monday, January 24 from 3:00 to 4:00 PM. We do host these calls every two weeks, just to remind you about that. And then, of course, if you have any training or workforce development ideas, please send those to labtrainingneeds@cdc.gov. And another reminder about how to ask a question, please put your question in the Q&A box, not the chat box in this Zoom webinar system that we're using today.

We are not able to track those questions in the chat box, but we can do that with the Q&A. So please if you feel comfortable, include your name and your email address. Apologies in advance if we cannot get to your question today. It could be for a number of reasons, mostly that we ran out of time. A second major reason is because we don't have the right subject matter experts on the call. We do ask that you submit questions that are related to laboratory testing. That is the purpose of these calls.

So questions about vaccines, we can't answer those. We can forward them but we can't promise that we'll get an answer for you. We do use the Q&A box also to track questions that are unanswered and try to help formulate agenda topics for future calls, so again please submit those questions through the Q&A button. And if you make a mistake and put it in the chat, we do have folks standing by to help and redirect and put you into the Q&A box.

And if you're with the media, please direct your questions to media@cdc.gov. And with that, just another quick reminder that the presentation material from panelists that are not affiliated with CDC do not necessarily reflect CDC's official position on that topic, and that includes any slides that are posted to our web page as well, that they're not CDC speakers. And with that, I think we're ready to go to our first speaker. Jessica Prince-Guerra is joining us today and is going to be talking about evaluation of SARS-COV-2 antigen testing in a community setting. And Jessica, I'll turn it to you.

JESSICA PRINCE-GUERRA: Good afternoon everybody and thank you Jasmine for your introduction. I am a Laboratory Leadership Service fellow at the CDC and today I'll discuss an evaluation that we conducted of the BinaxNOW rapid antigen test for SARS-COV-2 infection at two community testing sites in Pima County, Arizona during November of 2020. Next slide, please.

Here's a brief outline of what I'll be talking about today. Next slide.

I'll go ahead and start with some background and cover some background on testing and the reasons for the evaluation. There's multiple strategies that can be used to prevent the spread of SARS-COV-2, the virus that causes COVID-19. And this talk will focus on testing. Testing to rapidly detect and isolate infectious individuals is important for reducing transmission of SARS-COV-2. And it's important to have both a sensitive and specific test to be successful in these prevention strategies. Next slide.

There are different types of SARS-COV-2 tests. Real time RT-PCR testing, which detects the presence of viral RNA, is a highly sensitive assay that is typically used as the standard for comparison to other assay technologies. However, turnaround times can be long-- up to several days-- and testing requires a more complex laboratory and resources. On the other hand, rapid antigen tests detect viral proteins with the vast majority detecting the nucleocapsid protein. And rapid antigen tests can provide results in a fraction of the amount of time compared to real time RT-PCR testing and can be performed at the point of care and require fewer resources.

And thus these tests are an important tool for SARS-COV-2 prevention. However, antigen tests have been shown to be generally less sensitive than nucleic acid amplification tests such as real time RT-PCR, which can make interpretation of results difficult. Next slide. The BinaxNOW rapid antigen test is one type of rapid antigen test and it's conducted at the point of care and as a lateral flow assay, and results are read visually within 15 to 30 minutes.

This particular test received FDA emergency use authorization, or EUA, in August of 2020 and was authorized for use in symptomatic persons within seven days of symptom onset. At the time that this investigation began, the federal government had recently purchased 150 million of these antigen test kits and were distributing them to states to increase testing capacity. Next slide. At the time this investigation began in November of 2020, Abbott-- the manufacturer-- had validation data for this test for only 102 individuals, all of whom were within seven days of symptom onset with suspected COVID-19 disease but there was not any available validation data from asymptomatic persons.

The reported sensitivity in this initial validation data was 97.1% and therefore the purpose of this evaluation was to fill this knowledge gap and to gain additional data on the performance of this test in a real world setting that included asymptomatic individuals. Next slide, please. Next slide. Therefore, the purpose of the evaluation was to assess the performance of the BinaxNOW antigen test compared to real time RT-PCR in both symptomatic and asymptomatic persons who were coming in for testing at community testing sites. Next slide.

To go over a few methods, we recruited 3,419 participants from two community testing sites in Pima County, Arizona during November 3rd to the 17th of 2020. Individuals were aged 10 years or older and they were individuals who had presented to the testing sites for real time RT-PCR testing. They were offered a concurrent BinaxNOW antigen test. And at the time of this evaluation, the SARS-COV-2 prevalence in Pima County was high, with a 7-day case rate of around 250 per 100,000 population. Next slide, please.

CDC staff administered an electronic questionnaire to participants via REDCap that assessed symptoms on the day of testing, the number of days since symptom onset, whether individuals reported a known exposure to a diagnosed COVID-19 case within the past 14 days, and the list of symptoms that were asked on the questionnaire were based off of the Council of State and Territorial Epidemiologists COVID-19 2020 interim case definition.

We also obtained additional demographic data from the Pima County Health Department. Next slide, please. Paired samples were collected by health care professionals at the testing sites. We first collected a bilateral mid-turbinate nasal swab according to the BinaxNOW instructions for use, followed by a bilateral nasopharyngeal or NP swab for real time RT-PCR testing. Next slide, please.

After collection, the nasal swabs were immediately tested on site by trained CDC staff using the BinaxNOW antigen test according to the manufacturer's instructions for use.

Positive BinaxNOW results and counseling regarding isolation recommendations were given to individuals by phone after collection, NP swabs were stored in phosphate-buffered saline at four degrees and analyzed within 24 to 48 hours. And the real time PCR testing was conducted by a commercial laboratory that was contracted through the county. And this commercial laboratory in their testing workflow used two different assays for the testing. Because of this, 75% of the samples in this evaluation were run using the CDC Singleplex assay and 25% were run using a different assay, the Fosun COVID-19 rRT-PCR detection kit.

Specimens with inconclusive or invalid test results from either the antigen or the real time RT-PCR test were excluded for analysis. Additionally, if either the antigen or the real time RT-PCR test had a positive result, the residual real time RT-PCR specimen was sent to CDC for viral culture. And samples were cultured by limiting dilution in Vero CCL-81 cells, observed daily for cytotoxic effects and wells that

exhibited cytopathic effects, the presence of SARS-COV-2, was confirmed by real time RT-PCR. Next slide, please.

Just to present a few of our results. Next slide, please. Oh, sorry, can you go back one slide? A total of 3,418 paired specimens were collected and tested from participants ages 10 to 95. 24% of the participants were symptomatic at the time of testing, which we defined as having one or more symptoms. Nearly one third of the participants self-reported Hispanic or Latino ethnicity. And among asymptomatic participants, 1.9% tested positive by the BinaxNOW antigen test and 4.7% tested positive by real time RT-PCR.

Among the symptomatic participants, the present positivity was higher, 13.7% by antigen and 21.3% by real time RT-PCR. Next slide, please. And the average time to results for the BinaxNOW antigen test was 2.5 hours, compared to an average of 26 hours for real time RT-PCR results reporting. Next slide, please. Among the 827 symptomatic individuals, the sensitivity of the BinaxNOW antigen test was 64.2% and the specificity was 100%.

And among the 2,854 asymptomatic individuals, the sensitivity was lower at 35.8%, but specificity was still relatively high at 99.8% with four false positives identified in this group. Next slide, please. And this graph shows the BinaxNOW antigen test sensitivity in samples from symptomatic participants, categorized by the number of days and symptom onset on the x-axis. And in samples collected from individuals who are within seven days of symptom onset, the BinaxNOW antigen test sensitivity was around 70%. And sensitivity was lower in samples collected from individuals presenting for testing after seven days of onset.

Between 8 to 10 days, sensitivity was 50%. During 11 to 14 days, the sensitivity further dropped to 37.5%. And that BinaxNOW antigen test did not detect any real time RT-PCR positive specimens in samples from individuals who are 14 days past there is an onset of symptoms. Next slide, please. And this slide shows viral culture results in those samples that were positive for either the antigen or the real time RT-PCR tests that were tested at CDC for viral culture.

And we found that culturable virus were recovered from 35% of the total samples in this group. In samples with concordant positive antigen and real time RT-PCR results, culturable virus was recovered from 57.8% of the samples. And in the 124 samples that were antigen negative and real time RT-PCR positive, 11 or around 9% had culturable virus detected. And there was no virus that was cultured from antigen positive real time RT-PCR negative samples. Next slide, please.

In this slide we've plotted the BinaxNOW antigen test results on the x-axis and the real time RT-PCR cycle threshold values on the y-axis. It's important to note that we've limited the analysis to the samples that were tested using the CDC assay, and we've done this for both symptomatic and asymptomatic individuals. The blue dots represent culture positive specimens, and the black dots represent culture negative specimens.

We found that the samples with lower cycle threshold values were more likely to have concordant test results between the BinaxNOW antigen test and the real time RT-PCR viral testing, where samples with higher CT values were more likely to have discordant test results. And this was true whether in asymptomatic or symptomatic individuals. The correlation between CT values and the amount of RNA in a sample cannot be used as a direct quantitative measure of viral load, which requires the use of a standard curve. But nevertheless, this analysis was informative. Next slide, please.

Among specimens with positive viral culture, we found that the sensitivity of the BinaxNOW antigen test compared to real time RT-PCR and specimens from symptomatic participants was 92.6%. It was higher than when we analyzed it in all specimens. And in those from asymptomatic participants it was 78.6%. Next slide, please. The inability to isolate virus from a clinical sample should not be interpreted to mean a person is not infectious and capable of transmission just because there are many factors that may limit the ability to culture virus from a sample. Next slide, please.

This evaluation has a few limitations. First, nasal swabs were used for the BinaxNOW antigen testing but NP swabs were used for the real time RT-PCR testing. Second, COVID-19 symptoms can be often non-specific and they're difficult to capture in questionnaires. This investigation evaluated the BinaxNOW antigen test and results presented here cannot necessarily be generalizable to other FDA-authorized SARS-COV-2 antigen tests and this evaluation was conducted prior to the emergence of SARS-COV-2 variants. Next slide, please. Next slide.

So in summary, we found that the faster turnaround time of the antigen test compared to the RT-PCR could be beneficial because it allows for rapidly identifying persons for isolation. We found that the BinaxNOW antigen test sensitivity was lower in asymptomatic than in symptomatic persons, but specificity was high across both groups. And finally, we found that the sensitivity was higher among viral culture positive samples but it's important to note that some antigen test negative samples also had culturable virus detected. Next slide, please. Next slide, please.

So a few key takeaway messages. To alleviate the negative consequences of false negative or false positive results that can occur with antigen tests, CDC recommends confirmatory testing with a more sensitive laboratory-based nucleic acid amplification test in certain situations, which is based on a person's pre-test probability, and that takes into account the person's clinical and epidemiological context. For example, confirmatory testing might be considered for a negative antigen test if a person is symptomatic or has had a known COVID-19 exposure.

And as such, CDC has developed two antigen testing algorithms to outline when confirmatory testing is recommended. One that is specific to congregate living settings and one that is specific to community settings. Next slide, please.

Despite lower sensitivity, the faster result of the point of care antigen tests compared to laboratory-based testing such as real time RT-PCR can lead to more rapid isolation of COVID-19 cases, which is important for interrupting transmission. Next slide, please.

This evaluation could not have been possible without all the collaboration between many partners, many of whom are listed here on this slide. But I would like to thank the Pima County Health Department, the Arizona Department of Health Services, and the different various CDC task forces that were involved with the implementation of this evaluation, as well as our field team and all the participants. Thank you.

JASMINE CHAITRAM: Thanks Jessica, for that presentation. I have a number of questions for you. Several have come through to the Q&A box and they all kind of have a similar theme. So I think I'm going to summarize it into one major question. And that is that this study was done some time ago, it looks like, from the date that's on some of your slides. And so does CDC have plans to repeat a study like this now with the new variants that are out there with Omicron-- and previously I think we missed the window for Delta-- but are there any plans to repeat the study now with these new variants and also are there any plans to do other studies for other antigen tests that are out there?

JESSICA PRINCE-GUERRA: I'm a little bit outside of the COVID-19 response currently, and so I'm unaware of current plans that CDC might have for retesting some of these for some of the variants. But I believe, looking at some of the updated FDA website pages, they have been collaborating with the NIH RADx to do a little bit of this type of testing.

JASMINE CHAITRAM: OK. Thanks. And I know that Tim Stenzel from FDA is on, and since we're on this topic right now I've asked Tim to chime in now if he could and just talk quickly about those NIH studies and what he's seeing with antigen tests. We're seeing a lot of questions coming through about antigen negative but PCR positive. Tim, can you make comments on that?

TIM STENZEL: Sure. Yeah, absolutely. Hopefully you can hear me OK. So we had been hearing a lot of anecdotal reports. And one of them was published as a preprint last week - Dr. Adam Simmons et al. out of the New York. We also noted the South African paper that described the fact that saliva may be better for Omicron detection, maybe in around 86% although the confidence intervals were wide versus saliva, which they estimated around 100%.

And the [South] African paper teased that out a little bit more and described the fact that in saliva, the viral loads may peak a little bit earlier than in the nasal swab. But eventually the nasal passage did peak, so there is also, I think, a misnomer out there. The FDA has never stated that antigen test positivity correlates with infectiousness, nor does antigen test negativity correlate with non-infectiousness. I think that's just a very-- the FDA recommends against use in that sphere.

As we've seen in Omicron, patients can be infectious even before symptoms. It's estimated one to two days before symptoms, they can start to be infectious. And antigen tests on the first day, even for other variants, are frequently not as positive as they are on the second day. When we look at data across the first five days of symptoms, antigen tests, typically the good ones typically perform pretty well. You would think in the first five days of symptoms, typically someone may be infectious.

So we want to be able to have antigen tests that detect that at a reasonably high frequency, and we've recommended 80% for that. Or if you didn't hit 80%, that you would do serial testing. So with regard to the more specific Omicron data that was collected by the FDA from NIH and the RADx variant task force, they have for a long time now when we had a new variant in the US or even on the horizon, we talked about how to make sure that the tests in the US are US authorized and can detect those variants.

We've done that for a number of variants now. So it's a pretty well-honed system where as soon as-- unfortunately, we still seem to have problems getting samples from outside the country. So we know Omicron was coming before it was detected here. We tried, but we were unable to get samples from outside the US. So we had to wait until there were samples in the US. The first samples we got were heat inactivated samples.

The FDA posted the information that at least on heat-inactivated samples for the antigen tests, we were able to test for those samples. We didn't see what we would describe as a red flag for detectability of Omicron. So that was good news. But heat inactivated samples, we are cautious not to overinterpret those because antigen tests don't see heat inactivated samples, they see live virus samples. So the next wave of samples that we received at the variant task force for testing were live.

There were nine samples, so it wasn't a lot of samples. And they were QCed, or there were nine, rather, that passed QC and were ultimately pooled. They were high viral load, low CT samples. So the pool generated at its most concentrated level, 19. A CT of 19. And then step wise, once CT dilutions were made and we lined up antigen tests, we tested on the dilution series. And then we compared to similar dilution series that we had done for Delta and B.1.2.

And what we saw was that there appeared to be loss of sensitivity at a lower CT for the antigen test in general. It didn't really matter which antigen test it was, it looked to be across the board. The CT levels-- and these were all nasal samples-- they lost sensitivity earlier. So we're in the process of trying to confirm that. We did update our Omicron variant website at the FDA to say that while we believe that in general, antigen tests can detect Omicron, it may be with less sensitivity.

So we are in the process of trying to confirm that with additional wet bench testing. NIH has also agreed to open a new arm in one of their ongoing antigen test studies to do daily PCR and antigen testing. We're hoping that gets stood up really fast so that we can understand in a very controlled way what the performance of antigen tests are early in Omicron. So do stay tuned. We hope to have more information. That's about all that I can say right now.

JASMINE CHAITRAM: Thanks, Tim. That was great. I think another question/comment that came through in the Q&A box was, “What's the utility of antigen tests in a screening program if we are observing less sensitivity?” I think Jessica's point that she made towards the end of her presentation about rapid results and the ability to have information quickly is helpful, especially in a screening program and I think she also gave some recommendations that if an individual is exhibiting symptoms or has been

exposed, or there's concerns or questions about the actual result from that antigen test, that confirmatory testing may be necessary.

And so I think you need to take all of that into consideration when setting up a screening program. There was one other question that came through, Jessica, that I wanted you to answer real quick before we move to our next speaker. The question was about the time to result. I think you showed a slide where you said possibly two and a half hours for time to result in the study. However, the BinaxNOW antigen test does have a much shorter turnaround time for actual results. So can you talk a little bit about what that two-and-a-half-hour window was about?

JESSICA PRINCE-GUERRA: Right. That's a great question. And so from the time that you start the test to when you read it is 15 to 30 minutes for the IFU. However, the two and a half hours encompass the reporting aspect. And at this particular time the commercial laboratory that we were working with didn't have a mechanism for electronic reporting and a lot of their patient population didn't use electronic reporting. And so we had gotten the feedback from the county and from the commercial laboratory to do the phone call type of reporting.

And so that is what led to that 2.5 hours. And I think with the evolution of time and implementation of reporting mechanisms, I'm sure that this time would have decreased but because we were just starting this evaluation with a newly implemented antigen test the results were about 2.5 hours.

JASMINE CHAITRAM: Thank you so much, Jessica, for joining us today. We're going to move to our next speaker, Ila Singh from Texas Children's Hospital talking about TRUU-Lab Name Initiative. And I'm not going to say too much about it because I'm sure she's going to cover what that all means. So Ila?

ILA SINGH: Thank you. Thank you very much, Jasmine. So we're going to talk about TRUU-Lab Names Initiative, a step towards standardization, interoperability, and understanding focused mostly on SARS-COV-2. Next slide, please.

So I'm going to cover TRUU-Lab's goals in brief, talk about what we've done in identifying and categorizing common problematic names. We finished our first survey of 200 clinicians, and we've gone live for the second survey. And a little bit about what we are going to do next.

I'm not going to talk about what we have previously covered with the CDC, such as why naming problems exist or what are the safety issues related to names, what are our current practices to deal with bad names, and I have no conflicts of interest. I always like to start with a case. We had a case of measles and no one could find a lab test for it. And-- hey Jasmine, is this a PDF or are you using a PowerPoint presentation?

JASMINE CHAITRAM: This should be the PowerPoint slides that you sent for us.

ILA SINGH: OK. Because there were some animations that are lost. And that will be important for some of the slides that I'm going to use.

JASMINE CHAITRAM: Sorry about that.

ILA SINGH: Do you mind if I use my own here? Would that be a problem?

JASMINE CHAITRAM: No, that's fine. If you want to quickly share your screen, I'll stop sharing.

ILA SINGH: I'll do that. Perfect. Great. So no one could really find this test, and eventually it was there under Rubeola IgM. And I like to use this case because no amount of nerding out on LOINC codes would really help the commission in finding this because a lot of people have forgotten that measles is caused by Rubeola-- which is a good thing, I guess-- and I like to remind myself that there is a patient behind each of these decisions we make.

So TRUU-Lab is an initiative that I started about three years ago. It aims to bring together health care providers, professional societies, industry groups, and federal liaisons to address problems caused by ambiguous, incomplete, and non-standard lab test names. And our goals are to generate consensus names for existing lab tests, to generate a consensus guideline for test naming, and to promote the adoption and implementation of these.

We have a lot of members. You'll see I'm not going to go through all of them, but you'll see that there's a lot of professional societies, EMR, LIS, and terminology groups - LOINC, of course, reference labs, instrumentation makers, a lot of clinical pathologists and scientists. And it's very hard to keep these up to date, so I'm very sorry if you're a part and your name is not here. Federal liaisons, the CDC of course, is super important for many reasons, which I'll get to. The FDA and CMS, and then we have some international partners, some of whom are very good about coming to our meetings despite the time difference.

So the CDC are grateful to Jasmine, Nancy Cornish, MarBeth Gagnon, especially who has been involved since the very beginning of TRUU-Lab. Reynolds Salerno, Param Sandhu, and Monica Toles. Thank you so very much for your partnership. So one of the first things TRUU-Lab did-- and this will be obvious in a minute why I'm saying this-- is that we did a large survey to find out what were problematic names. And then with the help of Dr. Gary Procop, who's part of TRUU-Lab lab and who's now the president of the American Board of Pathology, we classified those into more or less 10 groups.

So there are difficult names-- like vitamin D; 25-hydroxy;1,25-dihydroxy-- ambiguous names, like all three of these names are for the exact same test. There are confusing abbreviations, like estimated glomerular filtration rate versus epidermal growth factor receptor, both of which usually show up uppercase in the electronic medical record. There are synonyms-- all three of these refer to the same test-- and there are brand names.

And if you wanted to change QuantiFERON gold testing to its more generic name, interferon gamma release assay for tuberculosis, you have a lot of trouble with your clinicians being able to find the test. There are similar sounding names, like Factor V Leiden, which is usually involved in clotting, versus when Factor V levels are needed is when the patient is bleeding. And they look very similar. There are common variations. Again, all of these are the same exact test but very different names. The confusing terms-- so we know that when people say free PSA, we mean it's a free form of PSA unlike a bound form, and yet there are several people who thought that is a free test that comes with no charge.

We pathologists like to give details. We like to tell people this is a LC-MS/MS test, liquid chromatography tandem mass spec. No one knows, and it seems no one cares. Then there are limitations of EMR and LIS. There are character limits. Every respiratory virus panel is different because different manufacturers make different panels and it's really hard for the clinician to know which panel has what. And it's hard for people to see an algorithm. How is the lab going to decide what they're going to do next? And then there is same exact analyte, but two different conditions in which you use it. And how do you convey that information?

So all this becomes important because as you're making names, why there is a confusion ends up determining what kind of fix you want to put in the name. So creating good names, traditionally names are chosen by lab directors without any input from people who use them. And so one of the things TRUU-Lab decided is, let's ask the people who use the names. That is, clinicians of all kinds. And clinicians' idea of a good name is colored by their own experiences, good or bad. And clinician experiences vary an enormous amount.

So let's just take HIV RNA test, quantitative. Different labs call it very different things, and you can see the names here. “HIV-1 Quantitative, Real-Time PCR”. Another lab is calling it “RT-PCR”. You know that's not real-time PCR, RT. Then there's the LOINC recommendation, which is “HIV 1 RNA NAA+probe”, and then there is the Mass General folks who were asked what name they want to see and they wanted to see “viral load” in there.

And they did not want RT-PCR, just PCR. Viral load PCR for HIV. Now, it's good to see that nobody calls it an AIDS test. And compare that with the SARS-COV-2 test that I'm going to talk about in a little bit, where people seem to prefer to call it a COVID test. So we were fortunate enough to get a grant from the CDC, a contract between the CDC and Brand institute. Brand Institute is involved in naming 80% of pharmaceutical products in the world. Both generic and brand names.

And they have a lot of experience doing surveys for safety, for names, and so they were super good partners for us. And for our first survey we surveyed 200 clinicians for 100 each for a named survey and a failure mode and effects survey. And these were folks who use tests quite a bit, so emergency physicians, pediatricians, OB-GYNs, family and general practitioners, nurse practitioners, and physician assistants. And they had a lot of experience as well, several years of experience.

So each survey had two structural parts. The first one, we gave a clinical scenario for which they chose appropriate lab tests and I'm going to show you that for SARS-COV-2. This was the unaided survey. On the second one, we provided background information about the test and then asked them questions about what would make an ideal name, and we call this the aided part of the survey. And the reason we did it this way is that having the aid first avoids provider responses that are driven by prior knowledge and experience.

So if your place calls something glycosylated hemoglobin for hemoglobin A1C, even though glycosylated is wrong-- that is not glycosylated protein-- you would tend to pick that as the right answer. So it also ensures that providers are making informed decisions and It reaches intuitive test names that we anticipate will be widely understandable. So here's sort of what our unaided survey looked like. A 40-year-old woman presents with fever and shortness of breath. She's not vaccinated against COVID-19. You would like to test her for potential SARS-COV-2 infection.

Now also remember that this survey was done in August, September of last year. So antigen tests were really sort of more in the purview of NBA players and not so much outside of that. So which of the tests listed below would you order? And please rank up to three tests listed below that best communicate exactly what you want. So for the test that best communicates select one, for the second test select two, for the third test select three.

And then we gave them a whole bunch of choices, like a dozen choices with SARS-COV-2 nucleic acid and various forms, antibodies, as well as antigen. And we did this survey not just with SARS-COV-2, but we did it for different tests, and here I'm showing you this. And really a lot of people chose incorrect answers for almost all of the tests we surveyed. So we had vitamin D testosterone, anti 10a, and COVID-19.

And so the yellow bars tell you that there's at least one incorrect choice. So if you just focus on testosterone here, almost every clinician had out of the three at least one incorrect choice. And then for testosterone-- this is especially bad-- that there were about anywhere between 20% to 40% of clinicians who chose no correct answers. They only chose wrong answers. COVID-19 on the surface looks better than that, and it is better than that. But if you dig deeper-- so again, at least one incorrect answer. 76% chose at least one incorrect test name. So either they chose sequencing or antibody or quantitative RNA, there were many options.

At least one of them was wrong. And 66% of selections were correct. So part of you thinks, oh, great. Unfortunately that's about equal to chance. So 66% of the choices were correct. So clinicians were choosing tests not much better than chance by chance. And pediatricians and physician assistants did worse than chance. And 10% of OB-GYNs and pediatricians chose only incorrect tests. So really, lab test names are a problem.

And further analysis of this unaided survey is that the most commonly chosen option was the SARS-COV-2 RNA by RT-PCR, which is great. We like that. And then the next most commonly chosen answer was

rapid antigen test for COVID-19. Remember we were asking for diagnosis of COVID-19. Names containing PCR, 46% of selections were chosen much more frequently as names containing NAAT. 46% versus 20%. And names containing rapid were chosen more frequently than as that-- just explained by chance alone, 17%.-- but offered only 10% of choices. Now the aided survey.

SARS-COV-2. This is just a little bit of detail about the disease, the virus, and then the viral RNA, the antigens, and I'm sorry but the antibodies-- there were a couple of lines on that that seem to have got cut off. But you can't give them a textbook, so you're sort of giving them really as little as possible, but enough so that they can make informed decisions with the rest of the questions. So which components of the name are most important? Analyzing here from a lot of-- so the top choice was name of disease, COVID-19.

OK. And this is in stark contrast to vitamin D or testosterone where people preferred the actual name of the target. And the close second choice was indication for testing. Example, for diagnosis of COVID-19 or for MIS-C. So if I combine their first and second choices-- this is choice number one, choice number two. And if you add them up, the time for result rapid comes up very close, even though it's not anybody's first choice but people want to see that somewhere in that test.

Name of disease is, again, 20. An indication for diagnosis. So these seem to be the most common things that people want to see in their test name. And then others are method, RT-PCR, or actual name of target. Much lower down was a simplified virus name, specimen type, whether the test was qualitative or quantitative, or warnings against inappropriate use. So just a little bit of nuance that who you're surveying changes the answer you'll get, because depending on the specialty they want to see different things.

So ER physicians are in this pale blue, and they want to know an indication for testing. Whether this is a test for diagnosis, they like to see COVID-19 in there. Whereas OB-GYNs want to see the name of the disease against COVID-19, they are here in orange, and they want to know the time to result-- whether it's a rapid test or not, which makes sense. You have somebody in labor and delivery, you want a test that will give you a result in an hour or two, not something that will come back next day. So it's important in any of these things to know who's answering your questions.

And then if you want to see-- when you ask them what in a test name would be most helpful to differentiate between an antigen test and a molecular test, a little over a third of people said that they want to see the type of target in the name, antigen versus viral RNA. And about a third said they want to see whether an indication for use. This is a test for early exposure risk, versus a test for diagnosis. And then there were lower responses for these other questions.

Keywords - a lot of people want to see either COVID-19 or COVID, and then they want to see SARS-COV-2 or COV-2. Lower down are coronavirus, PCR, diagnostic, et cetera. So the lessons that we learned are test names are a problem. Respondents do not perform much better than chance when they are asked to choose between a bunch of tests. They need help. And the most widely preferred names for information within names for poor identifiers. Name of target, utilization age, such as indication for testing.

The actual name of target was preferred for testosterone and vitamin D, but the name of disease was more frequently chosen. So there are exceptions to all of this and this is because COVID test is now part of our daily lexicon. Nobody says SARS-COV-2 tests, I'm going for my SARS-COV-2 test. Doesn't roll off anybody's tongue. Indications for use were strongly preferred over warning against improper use when both options were given. Except again, there's an exception like vitamin D testing where the target names are complex, indications are also complex. Warnings against inappropriate use were much more preferred.

And so there isn't a one size fits all, but there are likely common patterns that will become clearer with subsequent surveys. Our next survey which has gone out, a survey for SARS-COV-2 antibody test, which as lab director here I can tell you there is enormous amounts of confusion about which antibody test to get. And we will be using results from these surveys to build better general guidelines for test naming, including for SARS-COV-2.

And the rest of the slides are really more about what we are going to do at TRUU-Lab, when we have guidelines and how are we going to implement this, and get these standardized names and the foundation built, about EMR and LIS and ultimately result in better interoperability. I really want to thank everybody involved in this. Jasmine, Nancy, MariBeth, thank you. And Param, Monica, thank you for first of all recognizing that this was an important thing that needed to be done, and then shepherding us through the whole contract process. And we of course thank our partners in the Brand Institute. Happy to take questions.

JASMINE CHAITRAM: Ila, thank you so much for presenting on this really important topic. We did not get any questions for you. Actually, we got one question for you. But in the interest of time, I'm going to send that to you offline to follow up on. It has to do with new names aligning with ICD-10 codes. So let's table that because I bet that's not a short answer. And I just want to thank you again for being with us today. Really appreciate your time and this information.

We are going to change our agenda around just a little bit to squeeze in our last two topics. The first speaker for the rest of the call will be Natalie Thornburg from the Laboratory and Testing Task Force, and she is going to give us the SARS-COV-2 variants update, and I believe she will be sharing her screen as well.

NATALIE THORNBURG: Thanks. Thanks, all. Can you see my screen all right?

JASMINE CHAITRAM: Yep, we can see it.

NATALIE THORNBURG: OK, great. So I'm going to go through and just show you the data that's on the Nowcast that posted last week on January 4. So the data as of January 4 shows the weighted estimates for the week ending 12/18, and then updated to Nowcast for the week showing 1/1/2022. So all regions

showed an increase for the weighted estimates between December 11th and 12/18 of the Omicron variant and a decrease in the proportion of Delta between those two weeks.

And then in continuing those trends in the Nowcast, we saw an increase in the Delta variant across the US between the weeks of 12/25 and 1/1 with a decrease in the Delta variant as well. When we go down and look at regional data, we see that all HHS regions-- and this is the Nowcast data ending 1/1-- all HHS regions are now showing a dominance of Omicron variant with the lowest region being HHS region 7 with an estimate of about 77%.

Confidence interval is between 58.5 and 89.7. And then there are several regions, two, four, and six, which are estimated to be at approximately 98% Omicron and a very small percent of Delta. New data I think is set to post tomorrow. That data will then have weighted proportions for the week ending in 12/25 and Nowcast estimates for the week ending in January 8. And that is all.

JASMINE CHAITRAM: Thank you so much, Natalie, for those updates. Appreciate it. And now I'm going to turn it over to Tim Stenzel with FDA. Tim, the rest of the time is yours. Sorry for the delay here, we're just on short time.

TIM STENZEL: Yeah, no problem. I had two questions ahead of time. I'll start with those. So the first one asked, “The FDA stated consideration for granting EUA status for high-throughput variant detection assays. The current assays that are available require updating in order to include new variants as they arise. When this happens what processes will be in place for the FDA for timely expedited re-review of targeted variant assays that were given EUA status when they have been so updated?”

The FDA, of course, welcomes EUA requests from test developers for high-volume genotyping and whole genome sequencing assays as well as other high volume molecular assays, central lab assays. Since genotyping tests are likely to require frequent updating or making updates as new variants arise, we encourage test developers to consider including in their EUA requests-- whether it's the original quest or a supplement-- a change protocol, which includes procedures, including validation methods and expected outcomes of that validation that a developer could use when modifying the test to detect emerging variants.

So including this change protocol in the EUA allows the FDA the opportunity to prospectively review how the developer would go about making the modifications. And if the FDA authorizes this change protocol as part of the EUA, the developer would be able to make those future changes without additional submission to the FDA. And we would probably work out a mechanism for that developer to notify the FDA. But the review is needed for authorization is the concept.

For those that want to update existing tests, I would highlight a recent example of one LDT developer who was not able to detect Omicron and in fact, the FDA had authorized them to distribute their reagents to a large number of health systems. That test developer worked very collaboratively with the FDA to fix the issue and ran the validation plan by us. And the total time from identification of the problem to

reauthorization by the FDA was a little over two weeks. It was a really good and collaborative effort that really serves the public health and the public health emergency.

Next question is “What specimen source provides the most accurate results?” Meaning less false positives or different results from the same technique. PCR, saliva, or nasal? Not exactly sure the total underlying reasons for this question, but there is a lot of discussion out there about sample type for Omicron and sample type for PCR and antigen tests. So the performance is dependent on the test, and we do expect now for new tests and new sample types to see validation so that we know the test works with that sample type.

And we've authorized many PCR tests using anterior nasal specimens to make it much easier for collection with more available supplies and at lower risk to those who are doing the nasal swabbing, versus an NP swab which usually elicits a cough or a sneeze. And we've also authorized a large number of saliva-based PCR tests and more saliva-based submissions are, of course, welcome. Antigen tests, however, are typically authorized on nasal samples. This is because they're very easy to collect, especially versus an NP swab.

However, there is one high to moderate complexity central lab antigen test that is authorized for saliva. We do recommend that all tests be used as authorized because we know how they perform on those given sample types. There is frequently data available in the authorization documents about performance of each sample type. I put in the chat the link to the FDA website. There are now well more than 400 authorizations, so it's really difficult to categorize that. But you can go there and look.

Of course, I talked earlier about Omicron and there may be a different tissue predilection. So I understand why the sample type question may be coming up. We have seen highly successful PCR tests with saliva, there's many out there. We've also seen very poor sensitivity with those methods for whatever reason, we haven't necessarily figured that out. Antigen tests typically at this point have performed very poorly on saliva specimens.

We have seen multiple, only authorized one. The reason for this generally poor performance is not known. There are also a number of PCR tests that are authorized for health care collected OP swabs or oropharyngeal swabs. This is a different sample type than saliva, may perform different for a given variant such as Omicron, we don't know. All sample types authorized for each test are again listed on the FDA website.

The FDA is open to more oropharyngeal, OP, submissions. So if you're interested in that and validating that, send them in. And while nasal and saliva specimens have been found appropriate for clinical testing in many EUA-authorized tests, NP swabs are generally considered to yield the most sensitive test results and therefore that is the preferred choice when you're using it as a comparator for clinical investigations and validating new methodologies.

And the FDA in fact has heard that some hospitals are still requiring NP swabs for their in-house testing. They believe that is probably going to be more accurate. Some of them may be switching, don't know, just hear that NP swabs are still being called for in-house. But finding data right now-- at least I'm not personally aware of data of the performance, say, of NP swabs versus saliva or OP swabs for Omicron. So we'll be on the lookout for that.

So it's a long-winded answer. There isn't a clear-cut answer either. Thanks.

JASMINE CHAITRAM: Thanks, Tim. We did have other questions in the chat box, I'll send those to you later since we're out of time. I do want to thank all of our speakers for being here today, and all of you for joining us. Our next call is on Monday, January 24 and I didn't mention this at the beginning, but I do want to wish you all the very best and happy New Year. And we will talk to you in a couple of weeks. Thank you.