

Agenda

Clinical Laboratory COVID-19 Response Call

Monday, December 13, 2021 at 3:00 PM ET

Agenda

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 - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **Resources for Accurate and Reliable COVID-19 Testing at CLIA Certificate of Waiver Sites**
 - Nancy Anderson, CDC Division of Laboratory Systems (DLS)
- **FDA Update**
 - Tim Stenzel, US Food and Drug Administration (FDA)
- **SARS-CoV-2 Variants Update**
 - John Barnes, CDC Laboratory and Testing Task Force for the COVID-19 Response

JASMINE CHAITRAM: Hello, everyone, and thank you for joining the Clinical Laboratory COVID-19 Response call. Today is Monday, December 13. We've got just three other agenda items, but I think we're going to have-- I'm expecting quite a number of questions. I'm going to try to do my opening remarks quickly so that we can get to our first speaker.

Before we get into all of that, though, just a reminder that these calls are hosted by the [Division of Laboratory Systems](#) at CDC and we've been doing these calls now for quite some time. Our focus is on helping external laboratories of clinical and public health in a number of topic areas, including quality and safety, training and workforce, informatics and data science.

OK, everybody. I'm back. Sorry, but I'm off camera. As I was saying-- let's go to the next slide. OK, so just a couple of reminders before we get started. We do have our [Preparedness Portal](#) and we can have all of our information here. All of our previous calls, the transcripts and such can be [found here](#) as well as slides from previous calls. We also have an archive for all of our LOCS messages. And because these are not my slides, I'm going to ask George to help me out and go back to the beginning, because I had two other announcements. Second slide. Keep going. There were two slides on the bio safety page.

Ah. Yeah, OK. So just a couple of things we wanted to tell you about, which was that we put new guidance up on the [biosafety page](#) for over-the-counter tests that are used in high volume and point-of-care testing settings. And we've gotten a lot of questions about how to dispose of these tests when they're used in high volumes. A lot of the over-the-counter tests have been authorized to be used at home in single use sort of scenarios. But now that we're seeing that employers and other facilities are giving them out and they're generating a lot of waste, so we added some additional language there.

We also wanted to draw your attention to the new [Omicron web page](#). And this is not-- this page has been specifically targeted towards the public. It has general information, but you can find some good information here in addition to the variants page, which Dr. Barnes will present on a little bit later. And then a couple of reminders as usual. Our next call will be on Monday, December 27. Yes, we are having a call right after the holidays. I hope that's not an inconvenience for folks. But we do feel like it's

important to keep that call on the calendar due to the Omicron variant and any updates that may be necessary to provide you with at that time. Also want to talk about our email for providing information about education and training needs. It's trainingneeds@cdc.gov. Please send any of those requests there.

And then finally when you're asking a question, please use the Q&A button and not the chat. We want to be able to capture the question as well as your email in case we don't get to the question today because of the number of questions, or because we don't have the appropriate subject matter experts on the phone. Again, I do apologize for the technical difficulties this afternoon. Not sure what happened on my end, but we're still here and we will keep on going with the call.

And just a reminder that-- and we don't have anybody outside of CDC except for Tim. But remember that when you go and look at slides from previous speakers that the presentation may not necessarily represent the CDC's official position on that subject. And so just be aware of that.

And with that, we will go to Nancy Anderson, who is with the Division of Laboratory Systems. She is the Senior Advisor for Clinical Laboratories and she's going to be talking about accurate and reliable COVID-19 testing and CLIA Certificates of Waiver, and resources that we have for those facilities. Nancy, go ahead.

NANCY ANDERSON: OK. Thank you, Jasmine. Yeah, and I see my picture, so it looks like my video's working so I will get going here. As we've seen since the start of the pandemic, rapid testing that's performed in point-of-care testing sites under a CLIA Certificate of Waiver has become a very critical part of the response. As of the beginning of December of 2021, this year, the FDA has issued 64 EUAs for tests whose intended use includes laboratories or other testing sites with a Certificate of Waiver. And this total number includes 17 molecular assays, 34 antigen tests, and 13 serology or antibody tests for SARS-CoV-2.

As a result of all this increased testing in non-traditional settings, there's an increased need for guidance and education of the personnel who perform the testing, especially since many of these people do not have formal laboratory training. What I'm going to do quickly today is highlight some of the resources that CDC has made available for these Certificate of Waiver testing sites. Next slide, please.

On this bar chart, you can see the proportions of the various CLIA certificate types that have been issued since CLIA first became effective. And if you look at the darker blue segments at the bottom of each bar, the number and percentage of Certificates of Waiver issued over time has gradually been increasing at a fairly steady rate until you look at the point in time from 2019 to 2021 where there has been quite a significant jump in CLIA Certificates of Waiver. Certificate of Waiver sites now total over 260,000 laboratories and other facilities and they make up over 80% of all CLIA-certified laboratories. Next slide.

This slide and the one next to it give you some more detailed looks at the Certificates of Waiver that have recently been issued. This one shows the total number of Certificate of Waiver sites between 2018 and

2021, and you can see there was just a very small increase between 2018 and 2019. And then the number increased more significantly in 2020 and 2021. Next slide.

This is also a similar bar chart, but this one focuses on the new Certificates of Waiver for the same years. And you see the same type of increase. Since the start of the pandemic, there have been more than-- a total of more than 50,000 new Certificates of Waiver in laboratories in a variety of facility types. Next slide. With this rapid growth of waived testing in some very non-traditional testing sites, questions and concerns have been raised about the quality of testing and the reliability of those test results. And as many of you know and as is shown on this slide, CLIA has very few requirements for testing performed under a Certificate of Waiver.

Basically the site needs to enroll in the CLIA program, pay their fee and obtain their Certificate of Waiver. Of note, I will say is that CMS is temporarily exercising enforcement discretion under CLIA for SARS-CoV-2 point-of-care testing when a facility or site has applied for a Certificate of Waiver but has not yet gotten their CLIA number and their CLIA certificate. So the site can test and report patient-specific results as soon as they have submitted their application to the state agency.

The only other CLIA requirement is that for waived testing, laboratories or facilities need to follow manufacturer's instructions for performing the test and no modifications can be made to that test without losing the waived test status. There are no personnel requirements or other CLIA quality standards for waived testing, and Certificate of Waiver sites are not routinely inspected unless there's a complaint, or unless it's found that those sites are performing testing that is not waived. Next slide.

As a result of the concerns raised about the quality of waived testing going back many years before this current pandemic, based on recommendations from the Clinical Laboratory Improvement Advisory Committee, CDC developed a number of free, educational resources to promote voluntary good lab practices for accurate and reliable waived testing. All of the booklets and the posters that you see here, which are available in both English and Spanish, can be accessed or requested through the website, which is shown on the [link](#) on this slide.

CDC also has the "Ready? Set? Test!" online training that offers free continuing education credit. And that image is on this slide as well. Since March of 2020, CDC has distributed approximately 3,000 booklets that have come in by request through the website. And since the 1st of January 2020, more than 6,100 individuals have registered to take the online training. This is approximately double the rate at which the training was previously taken and completed. Next slide.

Now I have several slides just to give you a little bit more details about each of the products that you saw on the previous slide. The "Ready? Set? Test!" booklet. What you see here is the most frequently requested and used resource. And this booklet is designed for those people who are actually performing waived testing wherever that testing is taking place.

The information in the booklet covers the entire total testing process and it provides practices that should be followed before, during, and after testing. It also includes a number of charts, templates, and some logs that can be adapted and can be copied and printed and used by waived testing sites. The booklet and the related poster, as it says here and as I mentioned before, are available in both English and Spanish. Next slide.

Similar to and based on the “Ready? Set? Test!” booklet, the online training is a resource promoting good testing practices for individuals who perform waived testing. And the nice thing about this course is that it offers free continuing education credits for laboratory and other health care professionals. Physicians, nurses can also get continuing education credit. And this is a slightly different [link](#) on this slide, which will take you directly to a site where you can access the training. Next slide.

The “To Test or Not to Test” booklet is a little different from “Ready? Set? Test!” in that this one is geared for individuals who are responsible for setting up a Certificate of Waiver site or people who oversee testing that is performed at the point-of-care site under a CLIA Certificate of Waiver. In this booklet, there is information related to regulatory requirements, determining the location for testing to take place, training of testing personnel, and then other resources related to quality of testing.

This booklet also does contain helpful tips, reminders, and some additional forms that can be adapted for use in Certificate of Waiver sites and printed off. And just like the “Ready? Set? Test!” this booklet is available in both English and Spanish. Next slide.

If you go to the [CDC waived testing website](#), you'll also see there's a supplement to the educational booklets and online training. This is a checklist that can be used by waived testing sites to perform a self-assessment of their testing practices. The checklist includes questions that correlate to the information in the “Ready? Set? Test!” and “To Test or Not to Test” booklets, and it is in PDF format that can be downloaded and printed and used to take notes on. Next slide.

Those are the specific waived of testing resources that we have on our Division of Laboratory System website. Now let's take a look more broadly than just that website and talk about what is found on the CDC'S COVID-19 pages that are a valuable resource for guidance related to point-of-care and rapid waived testing for SARS-CoV-2. The [point of care and rapid testing page](#) does provide information on the regulatory requirements for performing this testing as well as how to properly collect specimens and report test results to public health.

It has links to a number of other resources, including several infographics that are highlighted on the next page, or the next slide. This page was published in October of 2020 and at this time, it's had over 343,000 total views with 242,000 views in 2021 alone.

Now we've gone on to the links for the infographics that are linked to the point-of-care web page. And the first one highlighted is the [batch testing tips](#). This is good information to help improve specimen handling and processing when a laboratory or other facility is performing testing on more than one specimen at a

time and doing batch testing. There are also several infographics on this same page on [nasal mid-turbinate](#) and [nasopharyngeal specimen collection](#). And these infographics include illustrations and some step-by-step instructions about how to collect these specimen types. Next slide, please.

This is another page with guidance on [antigen testing](#), which is intended for clinicians who order or who receive antigen test results and/or those who perform rapid antigen testing at a point-of-care site or in a laboratory. This page was published in August of 2020 and it is one of the most frequently visited pages related to testing. It currently has over 3.9 million total viewers with 2.5 million views in 2021 alone. Next slide.

One last bit of information about resources for antigen testing. The three devices that you see in these infographics are rapid antigen tests that are commonly used in point-of-care sites and labs with Certificates of Waiver. And these are also linked. You can get to these from the [point-of-care testing page](#). Each infographic has tips based on CDC experience with these devices for before, during, and after testing and they are intended to help ensure that the tests are performed correctly. Next slide, please.

Moving on to biosafety, Jasmine already gave you some updates and has shown you some pictures of this slide. Biosafety is also important in point-of-care and Certificate of Waiver sites and may be something that is fairly new to people and facilities that are performing this kind of testing. In general, the [web page](#) has biosafety guidance important whenever a facility is handling specimens and performing testing, and this page also has a section that's specific for point-of-care waived testing. It does also include information on waste management, as Jasmine gave you the update, and on packing and shipping specimens. This page has been available since January of 2020 and has over 707,000 total views, with 129,000 views in 2021. Next slide.

One of our most recent website additions published in June of this year is this page, which specifically provides [risk management information for point-of-care testing sites](#). The information that you can find here focuses on specific biological risks when performing testing in these types of settings, which are primarily Certificate of Waiver sites. Next slide.

As with all CLIA-certified laboratories that perform SARS-CoV-2 testing, point-of-care, and other Certificate of Waiver sites are required to report both positive and negative results of diagnostic and screening tests to their appropriate state or local public health department. On this [page](#), you can find information on who needs to report, how to report, and what information needs to be reported to public health. This page has been available since May of 2020 and has had over 487,000 total views with 182,000 views in 2021. And next to the last slide, I believe.

Finally, in addition to [CDC](#), this is just a reminder that [FDA](#) and [CMS](#) also have a wealth of information and guidance online about CLIA waived testing and the COVID-19 response. And you have links on this page, which direct you to additional resources that are available and provided by all three agencies. And with that, I think we have one final slide.

The general slide with more information, where you can go-- the contacts for additional questions or information. With that, I am done and I have not seen-- I don't know if there are any questions.

JASMINE: Hey, Nancy. Sorry about that. I'm having a lot of technical difficulties today. There was a couple of questions for you. The first one is, and I think you may have covered this in your slides, but just repeating it would be great. Where can one apply for the CLIA Certificate of Waiver?

NANCY: All right. The CMS website, which was on the next to the last slide, has information for how and where a laboratory or waived testing site can go to get their Certificate of Waiver. They go through their state agency, but the specific, really good step-by-step instructions are available on the CMS website.

JASMINE: Great. And then this isn't really a question, it's more of a comment about the fact that pharmacies are doing more and more waived testing and that this is good information for them. And so we need to just do better with outreach to pharmacies to make sure that they're also getting this training and that they know these resources are available. Thanks for that comment. One other question for you, Nancy. Are provider-performed microscopy CLIA laboratories also exempt from accreditation surveys. There are no other moderate complex lab tests performed but performing waived EUA COVID-19 tests. I'm not sure if you can see that question.

NANCY: Oh, yeah.

JASMINE: I think it's-- can you see it, Nancy?

NANCY: Yes, I see it. And so yes. Waived testing is not-- I'm not sure if this is their question. But waived testing is not subject to inspection, regardless of where it's performed. And in general, PPM laboratories can perform waived testing. I'm not sure if that was the question asked.

JASMINE: OK. And then I know we're getting into some questions here for CMS, but another question is do private businesses need a CLIA to test their employees?

NANCY: If the information is being reported back to the person testing for health care purposes, a CLIA certificate is required.

JASMINE: OK. If my site applied for a CLIA waiver and provided the testing material intended to be used as different, does the clinic need to update? I think the question is they applied for a CLIA waiver but they're doing a different type of testing. So do they need to update their CLIA certificate? And most likely if they're doing some testing that's other than waived, the answer would be, yes, right?

NANCY: Right, right. Especially if they are. And I do believe if they're doing a different waived test, they are also supposed to report to CMS that they have added or changed the testing they're doing.

JASMINE: OK, great. Nancy, thank you so much. In the interest of time, I'm going to go ahead and move to Dr. Tim Stenzel from the FDA. Thank you again, Nancy, for all of that information. Appreciate it. Just a reminder to everybody that the slides will be posted. Lots of good links to web pages with lots of resources. So please visit the archives on the preparedness portal if you need that information. And Tim, we're ready for you to go ahead with your update. And there are a number of questions in the Q&A box for FDA as well.

TIM STENZEL: Thank you, Jasmine. I'm going to go ahead and share my screen to help walk through this. I have also put into the chat or the Q&A two FDA links. One for anybody who wants to [submit an assay for EUA authorization](#) and the second one that I put in chat was the [FDA mutation web page](#), which I'm going to now, as soon as I select the right screen.

All right. Hopefully you can see it within a few seconds. From the very beginning, the FDA has been looking at the possibility of mutations and then ultimately variants that would affect, in some way, test performance, primarily diagnostic tests at this point. But in the beginning, and we currently look at all tests, includes serology.

So we ask developers of molecular tests to submit the primers and probes sequences in their submission and to do in silico work to make sure there wasn't any warranted cross-reactivity with non-SARS viruses and also to do inclusion studies to make sure that the known variants and mutations, at the time of their submission, were going to be able to be detected at their assay, at least for circulating mutations and variants that were at the 5% level or above, or anticipated to be at the 5% level and above in total.

And so we have those sequences and have been monitoring at the FDA since then, and actively doing monthly searches starting in the summer of July 2020 and-- in the summer of 2020, and then we moved to weekly. Omicron is obviously really important to look at. And we have taken a look and we have identified, out of abundance of caution, a number of assays that-- where we've sent letters to the developers to do additional work.

We have started to receive responses. And to date, we have posted two molecular assays on our website, the Meridian Bioscience Revogene, which has not launched yet. So you can't even get it, but out of an abundance of caution, we have posted this information. And the Tide Laboratories assay, which is used in 33 labs in 16 states, although we don't think the testing is high volume.

Neither of these assays do we believe-- which are single target SARS-CoV-2 assays do we believe will be able to test positive on Omicron samples. We are continuing our work with molecular and antigen tests. And as we get additional information where assays may struggle, or not detect, we will post that information on the FDA website as soon as we have confirmed that and we can get it posted. I recommend checking this link that I sent on mutations at a regular basis, especially regarding Omicron, which our work in this area is ongoing and very active.

Obviously with molecular assays, we can do a pretty good job of predicting whether an assay has any mismatches with Omicron. And even if there are single nucleotide mismatches, if that's likely to impact the assay or not, and we do triage. The level of concern and the highest level of concern assays, obviously, get our first attention. And obviously these two assays rose to the top. And we were able to get them posted already.

Molecular is relatively straightforward. We don't think it's the end of Omicron updates for molecular assays. So do keep listening and watching the website. Then on antigen tests-- although on molecular we don't think there's any widespread problems. But there will be perhaps some additions. At this point, we don't think there are going to be high volume assays, if any.

Going to antigens. So antigen analysis of the impact of variants and mutation is obviously for those who understand, the challenges that we might have is much more challenging. We prefer to have the variants tested on actual virus from a culture, can be inactivated, or from actual patient samples. The in-silico analysis that we can do can sort of say, well, for those developers of antigen assays who have mapped the epitopes and their antibodies, we can line up sequences and say are the mutations in the variants or any mutations within the epitope or not? And obviously if something were to be inside an epitope, there would be a clear concern.

And then also if something is just outside an epitope, we have no idea yet whether or not there might be a tertiary change in the molecular structure that would render the assay less sensitive or unable to detect any given mutation or variant. We actively look on antigen tests with bioinformatics first. And we triage those. We work with RADx NIH Variant Task Force and CDC to do this testing in the lab and under the observation of government oversight and we test. We also engage the developers and ask them to submit information. But we frequently want to confirm performance, particularly for antigen tests, under the auspices of the US government so that we can assure everyone of what we think is going on. One of the challenges that we have with Omicron is there are so few positively identified sequenced Omicron samples in the US right now. We've tried to get samples internationally. That has been a challenge. And so as samples are identified in the US, we're trying to get them into this testing program so that we can test according to the triage, the antigen test, to confirm performance with Omicron. That's the status of antigen. I cannot today tell you that any antigen tests will fail Omicron. But the investigations are ongoing. I cannot promise the results of that and neither can we be sure that antigen tests will fail. It's unfortunately an area of active investigation.

We are looking closely at any complaints that come into the FDA directly, or to the companies themselves, which then get transferred to us. And I said, we're engaging all fronts with all developers in this area.

All right, I want to move on to identification of Omicron. And there are a couple of ways that Omicron can be at least-- potentially be identified quickly using molecular assays. Most everybody has heard about the s-gene dropout. And the canonical assay here is the TaqPath assay, and there's more than 20 other assays that essentially copy that design. And we have listed those assays on this FDA website.

There are usually three targets in these assays. One of them is the s-gene and when a sample has a deletion 69 to 70 in the s-gene. The s-gene signal in these assays will essentially go to zero. But the other signals should be positive if it's SARS-CoV-2. That pattern, we're recommending, if possible, to have those samples sequenced to confirm whether or not it's Omicron, at least for the foreseeable future. And that's an important way to identify how quickly Omicron is entering the US and how wide-spread it is. The FDA will not object to assays that have this s-gene dropout from the labs that use these assays from reporting s-gene drop-out to their clinicians and patients. Let me say that again in a different way. The FDA does not object if you identify an s-gene dropout in one of the s-gene dropout assays and reporting that clinically. It doesn't mean it's Omicron, because there are Omicron-- I'll go into this later. There are Omicron variants and sub-variants that don't-- sub-lineages that don't contain the s-gene dropout. In particular, BA.2. BA.1 sub-lineage does have the s-gene dropout in the majority of cases, but not all. And BA.2 does not. So far, at last look, we don't have any of the BA.2 sub-lineage in the US, but we are anticipating that will arrive.

Rather the BA.2 lineage can be identified by an n-gene dropout. So we will shortly post two assays so far that we've found that are EUA authorized that will have a similar drop out signal as the s-genes dropout, except it will be an n-gene dropout. And this time, the deletion present in Omicron and is present largely in both BA.1 and 2 is the n-gene deletion 31 to 33. We have identified two assays and done initial confirmation that they will dropout the n signal for Omicron. And so stay tuned for that to be posted on the FDA website as soon as we can get it up there.

And so there will be two methods to identify a sample as Omicron potentially. And again, not all samples have n-gene dropout. But we believe at the moment that n-gene dropout is at least caused by the deletion 31-33 is unique to Omicron. And again, the FDA will not object if you want to report any clinical reports that there is n-gene dropout as seen in these two EUA-authorized assays.

I think I want to finish up on Omicron by saying that for a while now we have been open to receiving genotyping assays. We have-- because the variant determination is very complex and there's so many different mutations that are shared between variants, and there are a few unique variants that identify-- mutations within a given variant that identify it as that variant. Then n-gene dropout, for example, is one, but it's not present in all Omicron.

Whole genome sequencing is still probably the very best way to definitively state what the genotype is thoroughly and assign a variant status. And also, it gives you all the mutations that may be of interest. However, there are strategies that are being developed, and some may have already developed these and validated them. The FDA suggests if you want an EUA authorization for that that you submit that. The FDA has generated recommendations for genotyping validation. And if you send an email to the templates email address, and I can't remember-- yes, I already put that into a response to the Q&A what the template email address. So you can send a request for FDA recommendations on genotyping validation and get that information back from the FDA if you're so interested. Again, the FDA is accepting applications for high volume genotyping assays for review. I think that pretty much covers what I wanted to say, Jasmine. Open to questions. And I will look to the Q&A and answer online as long as we're online.

JASMINE: That's great. Thank you, Tim. I was going to ask you two questions since you mentioned sequencing. The first one is, is the EUA test submission still the same for those who are working on their CLIA whole genome sequencing validation after November 15?

TIM: If they're high-volume assays, we're going to accept them for review. If they're already validated and they were launched by November 15, they can stay on the market while they're reviewed by the FDA.

JASMINE: OK, great. And then one other one. Question is, where do we submit COVID sequencing data as notification for our CLIA validation that we completed in June 2021?

TIM: I might answer that question with an email address.

JASMINE: OK. OK, that sounds great. If you could type that in the Q&A, that would be helpful.

TIM: I'm just checking-- I thought I put it in there. I didn't press send.

JASMINE: Maybe you did. Oh, no. I don't see one. But if you want to, Tim, there's a number of questions not related to Omicron.

TIM: Yeah, Sergei submitted it at 3:02. And so I put the CDRH EUA templates email address in there.

JASMINE: OK, great. Thank you. I'm not seeing it on my end. But that's great. Thank you. All right. I'm going to go ahead and move to our last speaker because I think the updates from Dr. John Barnes are also really important today. And he's going to be talking about SARS-CoV-2 variants, regular updates the CDC gives, and of course, an emphasis on Omicron. So I'll just turn it over to Dr. Barnes now.

JOHN BARNES: Hi, Jasmine, and thanks, everybody. I'm just going to give a verbal update because the data that we have into the Nowcasting estimates, none of the Omicron sequences that actually were first identified actually made it into the data cutoffs to actually be displayed on that. So we don't have any SARS coronavirus Omicron variants actually in that Nowcast. And so it is-- as recent events have been-- recent updates have been at 99.9% Delta. Delta is still predominant variant, even though Omicron is on the news and everybody's minds at this point in time.

We do have sequences that have occurred, of course, in our new estimates, and those will be public tomorrow. And so those, I will just give you a word of caution as the Nowcast estimates always have pretty big error bars associated with them in the first set of estimates when we're trying to estimate a variant. And it really has to go with going from no incidence of a particular variant to all of a sudden finding sequences. Really trying to figure out what the overall slope of that line is, is quite difficult and requires a bit of backfill of data as we go on.

If you'll remember from previous updates we have, CDC-- the data that we have for those estimates is really filled in over several weeks, and there's about a two-week lag to some of the sequence data coming in from some of our sources. And so we really will get some backfill with that data. And so those estimates will be in flux over the first next little bit.

A couple of words about Omicron. As Dr. Stenzel said, we were using s-gene target failure to try to prioritize specimens at the beginning, and even opened up our extra surveillance that we have, our enhanced surveillance that we have, based on s-gene target failure that we originally put in place during Alpha. This we just transitioned out of as of Friday. The reason is we had an overwhelming support with that and a lot of specimens were sent to CDC for processing. We have several of those viruses in culture right now. We hope to have more empirical data on those viruses very, very soon.

And so we wanted to thank everybody for submitting those viruses in. That was very helpful for us to get those in so they can be evaluated in all the ways that we really want to see how well they're going to do with our vaccines and other questions like that. We have that. That data is still going to be made. We're hoping to have cultures very soon so we can do neutralization and other types of things.

We wanted to also stress that-- and kind of that during something where we can use a PCR method like s-gene target failure, or this new n-gene target failure that Dr. Stenzel talked about earlier, to try to maintain what we do for national surveillance as a random as sample as possible. This is really, really important for us in the tracking of variants as we go along. We have other variants that we're interested in and we're tracking, like the Delta variant AY4.2, which was the one that was in England right before Omicron that was trending up.

And then B.1.640 was another one that we're interested in that has some worrying mutations in the spike. We don't know what the proportionality, or how these variants will compete with Omicron, and so it's really important for us to make sure that we get things like s-gene target failure or n-gene target failure don't influence our numbers, if you will, that are run through sequencing, or anything like that.

I state that here so as you're sending things in for NS3 sequencing, please make sure that those are as random as possible and stick to the tenets of that procedure as well as we can. And then the second thing is if your assays were actually working on generating sequence itself to make sure that if you've used an s-gene target failure or n-gene target failure, if you could give us a heads up or make that in one of the comments or some of the associated metadata that will help us understand which of those-- why those may have been selected.

I also will point out things like travel history also tend to skew this data a bit as well. And so that it would be a consideration as well. With that, I'll hand it back over to you, Jasmine. Thank you.

JASMINE: Thank you so much. I do have a couple of questions that I'd like to ask you before we run out of time. The first one is, has BA.2 Omicron been reported in any other country?

JOHN: Yes. It's been reported-- actually, there was a case reported in Canada last week and then there was-- it's been seen in several other countries. Australia, South Africa, of course, most of Southern Africa. And then I think it's actually been reported in England as well.

JASMINE: OK. The next question is ORF1 is a common target in assays. Have any ORF1 dropouts been seen?

JOHN: I don't know any. That may be for Tim.

JASMINE: OK.

TIM: And if you ask that again, Jasmine?

JASMINE: The ORF1. Have we seen any ORF1 dropout?

TIM: No. No. It does bring up a topic I don't think we have time for today. But I did want to talk about, at some point, as more and more mutations and variants become known, what are the optimal molecular designs at this point in the pandemic. But I don't know of any dropout, submitting a dropout that would affect sensitivity of ORF.

JASMINE: All right. Thanks. And then another question, I guess, for Dr. Barnes, do we-- the CDC multiplex primer set I think-- have you seen any issues with the n-gene dropout with the Omicron variant? Tim just mentioned that n-gene is also possible.

JOHN: The CDC multiplex assays is not affected by that particular deletion mutation. Neither are the CDC N1 or N2 assay. The CDC N1 assay did have a point mutation at the probe that we have done a previous evaluation on but not really seeing that much of an effect on. But none of those assays actually span that particular set of amino acids that would have caused that particular drop.

JASMINE: OK, thank you. The next question I think is actually for Tim. The question is they're not clear on which vendors and target would cover a 31-33 deletion. Does FDA plan to list those products on their website as well?

TIM: Yes. We're working on those two known products to get them onto the website as soon as possible. That's been so ordered, and we're just waiting for the mechanics of the process to complete and then it'll be up. I can't promise when. I'm not fully in control of that.

JASMINE: Thanks, Tim. And then one more question, Tim, if we could squeeze it in right before we end here. Given that the s appears to be highly mutated among variants of concern, is the FDA guiding new developers against targeting the s-gene in their assay?

TIM: Can you ask that one more time again, please.

JASMINE: The question is, are you giving any guidance to developers about targeting against or not using the s-gene assay and the s-gene in future assays because we've seen it in variants of concern?

TIM: Yeah.

JASMINE: S-gene dropout.

TIM: Well, I can tell you that I'm grateful for the s-gene drop out and for the n-gene dropout assays right now, because they will help us identify Omicron.

JASMINE: Right.

TIM: But if it already has an s-gene and there's only two other targets, or maybe there's only one other target, then there's a greater chance that the assays could be falsely negative. So it's a complex situation and I don't have a perfect answer.

JASMINE: OK. And thank you very much to all of our speakers today. I'm going to wrap up the call here and again apologize for the technical difficulties at the beginning. We made it through anyway and hopefully the information was useful to all of you. We are planning to have a call on December 27. Apologies again if that's inconvenient. We do record our calls and then post them about a week later. So if, for some reason, you can't make it to that call, just visit our [Preparedness Portal](#) for the transcript and the slides for the December 27 call.

And then also if you are not receiving messages from LOCS, locs@cdc.gov, you can send us an email and we can put you on our distribution list to receive future communications from us. And with that, I just want to wish you all happy holidays and stay safe during this time, especially as you travel and visit with family. Thank you.