# Clinical Laboratory COVID-19 Response Call

# January 25, 2021

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**JASMINE CHAITRAM**: Hello, everyone. I'm Jasmine Chaitram with CDC. I'm the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems. Thank you for joining the Clinical Laboratory COVID-19 Response Call. DLS, the Division of Laboratory Systems, has been hosting this call since March of last year. And we want to welcome you today. If you've been here before, then welcome back and thanks for joining us.

I'm showing on the screen right now today's agenda. We've got a number of great topics to present to you today. Before we get into the agenda, I am going to cover a few announcements and a couple of housekeeping items.

And I also want to mention, for those of you that are new to the call, the Division of Laboratory Systems has been focusing on supporting clinical and public health laboratories in the area of informatics and data science, biorepository science, quality and safety, training and workforce development. And this has been going on for many years. We've also been doing preparedness and response activities, and continue to do that during the COVID-19 response, and serve as a liaison to the CDC Emergency Operations Center for clinical and public health laboratories.

And with that, I'd like to just give you my first announcement, which is that the Division of Laboratory Systems has also been involved in updating and providing new guidance on the CDC webpages. Most recently, we helped to develop at-home testing guidance. And this is really for the general public about at-home testing, and even about collecting specimens at home. So it may not be necessarily for your facilities and your laboratories, but we do want to get the word out there that there is information for the general public. So we would appreciate you just letting your friends, your colleagues, family know that there is information about at-home testing on the CDC pages.

Also, we continue to provide links to other important resources for laboratories. These slides will be posted on the DLS Preparedness Portal, which I'll show you in just a second. But just a reminder that we do post all of our transcripts and audio and slides from all of our calls, so you can find them there if you miss anything or if we're going too quickly throughout the call.

Here is a link to the DLS Preparedness website, where you can find the information from past calls. You can also find here links to other important COVID-related information, as well as all of our archived Laboratory Outreach Communication System (that's LOCS) messages. So if you want to go back to see a message and you can't find it, you can always find it on our DLS Preparedness Portal.

OK, a couple of other things. The next call will be on Monday, February 8th from 3:00 to 4:00 PM. We do hold these calls every other week. So that will be the time and date for the next call. We do want to hear feedback from you, especially on training and workforce development needs. And you can submit those to LabTrainingNeeds@cdc.gov. Likewise-- I think I've mentioned this before-- if you have suggestions for topics for these calls, you can submit those to LOCS@cdc.gov.

And finally, how to ask a question. There is a Q&A button in the Zoom webinar system, and we prefer that you put your question in the Q&A box. And if you're not shy, we would appreciate your name and your email. We do try to answer all the questions-- or not all, but as many as we can-- during the call. And if we cannot answer them during the call because of time, then we do try to come back and either answer them offline, separately in emails, or in future agenda items in future calls. So please submit your questions through the Q&A, and not in the chat box, and include your email address if you want us to get back to you, just in case we don't get to your question during the call today.

And then of course, if you're CDC-- if you're looking for-- if you're from the media, sorry, if you're with the media, please contact CDC Media Relations at media@cdc.gov. And if you're a patient, please direct your questions to your health care provider. And I think with that, we are going to go into our very first topic for today's call. And I want to introduce and thank Nadia Ayala-Lopez from John Hopkins Medical Institute for joining us today. And she's going to be talking about clinical laboratory result abnormalities in patients that have been hospitalized with COVID-19. Nadia, whenever you're ready.

**NADIA AYALA-LOPEZ**: Thank you, Jasmine. It is my pleasure to be here to discuss some of the findings that we're seeing across the US in patients-- and the world-- in patients that present to our health care institutions with severe COVID-19. There are several hallmarks that are beginning to appear in COVID-19.

This is something that we were looking at very early in the pandemic, what sort of markers of COVID-19 disease were appearing in these patients to be more prepared not just in the laboratory, but also to treat patients appropriately. And these markers that were beginning to show those markers of inflammation and coagulation and tissue injury. But this is three main

categories of where clinical laboratory testing has really shown differences in these patients with severe COVID-19.

So we are aware that COVID-19 has a strong inflammatory component, especially in patients that require hospitalization. So in bold are the markers that are most striking. Oh, I'm sorry, I'm on the inflammation slide. So one more slide. Perfect. Thank you. I will remember to ask you to switch the slides.

The first marker I want to discuss that we see often elevated in severe COVID-19 is C reactive protein, or CRP. This is elevated, as well as IL-6, interleukin 6. And that's in bold. As we know, a lot of therapies are coming out that inhibit this pathway. And also, other markers of inflammation that are elevated that we see are TNF alpha (tumor necrosis factor alpha), IL-1, IL-10, and IL-2.

Several studies show increases in ferritin in these patients, also due to the large inflammatory response and cytokine storm. An increase in neutrophils, in WBCs, is also found. However, this can be variable and depending on the disease severity and the progression of the disease. And we're also seeing large increases in procalcitonin. This can be due to secondary infection, but also within the large inflammatory response itself.

A striking feature that we are often seeing in these patients of severe COVID-19 is lymphopenia. Specifically, the reductions in CD3 positive and CD4 positive cells, and CD8 positive T cells. There are also proposed biomarkers to predict the severity of COVID-19. And those are IL-6 and CRP, are coming out as ones that are highly predictive for severity.

Also, what has been used in the clinic and has an observation to be useful is the neutrophil to lymphocyte count. Since we see an increase in neutrophils with a decrease in lymphocytes, a high neutrophil to lymphocyte count have been reported. And also, a low lymphocyte to CRP ratio is another one of those proposed biomarkers.

In a meta-analysis of 22 studies on hospitalized COVID-19 patients, lymphopenia and neutrophilia at admission were associated with poorer outcomes. So we're starting to see that not only monitoring the patients while they're in the hospital would be useful to use these markers, but it could also be predictive and helpful at admission to know how to manage patients going forward. And a newer marker that has been published is elevated red cell distribution counts at admission have been associated with mortality risk in COVID-19 as well. Next slide, please.

Another hallmark that we're seeing in severe COVID-19 is coagulopathy. So this is something that is appearing as abnormalities and coagulation, leading to venous and thromboembolic complications are being found in 10% to 25% of COVID-19 patients that require hospital care. Notably, D-dimer is increased in patients with COVID-19-associated coagulopathy. On the right, this is a graph from ICU patients and their D-dimer levels, and showing each specific data point

for each patient within the day of illness. So you can see the large spread, but we also see very high D-dimer values in these patients.

And this is also one of those predictive markers that D-dimer is associated with a higher risk of mortality. One study said about 18 times was observed when patients had D-dimer concentrations over one mg per liter. Also pointing to coagulopathy in COVID, we see prolongation in the prothrombin time, as well as a decrease in platelets. So this decrease in platelets may be mild, you know, 150 to 111. It really depends on the patient, or the platelets might be normal. So we're not seeing huge, drastic decreases in platelets at this point. But they may be decreased below the reference interval.

Also, fibrinogen concentrations may be either increased or decreased. This really depends also on the stage in the progression of the disease, as during the inflammatory response, fibrinogen may be higher, near or above the upper limit of the reference interval. However, right before death, it has been shown to decrease. Next slide, please.

Another hallmark of severe COVID-19 is the markers that show tissue injury. And these include liver injury markers, such as liver injury associated enzymes, ALT, alanine aminotransferase, and AST, aspartate aminotransferase. And when we see a diminishing in liver function, we may see a decrease in serum albumin levels.

Also, with COVID-19-associated acute kidney injury, we are seeing an increase in serum creatinine and serum urea nitrogen. And this is also one of those markers that have been associated with a high risk of mortality in COVID-19.

In some of the patients that have cardiac injury, you see an increase in troponin. And it has been reportedly seen in 7% to 17% of hospitalized COVID-19 patients. You also may see increases in lactate dehydrogenase. On the right is a depiction of the most common markers that are present and their associated organ systems that are affected.

Of course, this is just a very selected, very small list of different tissue injury markers. Right now, I'm reporting on what is coalescing as the most notable and also the most routine that are usually measured in a clinical laboratory. So there are lots of markers that may come out that are being reported on, either due to tissue injury, coagulopathy, or inflammation. And we are learning so much more in this space. Next slide, please.

So in conclusion, we have reports on various clinical laboratory findings. The main ones are that coalesce in the categories of inflammation, coagulopathy, and tissue injury. I also want to note that there are lots of other markers that are out there that are being measured in clinical laboratories. And these may or may not become more routine as we learn more about COVID-19.

So more studies are really needed on the associations of laboratory markers, as well as these predictive calculations and how they are associated to outcomes. As therapies to COVID-19

evolve, we'll need to understand these more. We'll also need to understand how these markers interplay with different comorbidities of COVID-19, and how well they're able to still be predictive and informative in a background of another disease state.

So these early observations and early papers that I'm reporting on are really instrumental in being able for laboratories to prepare to make sure that we have the resources on hand. Not just staffing, but also supplies to facilitate the testing and management in these patients that go beyond just diagnosis of COVID-19 and SARS-CoV-2 infection, but in management of the patients. So the ability of the laboratories to provide valuable, timely, and accurate testing in the setting of COVID-19 has been and will be essential in the management of the pandemic.

And these are my references. I know that they will be providing these slides later, if people want to read more on this topic. And you can also reach out to me @drayalalopez on Twitter. Thank you. And I'll happily take any questions that came in.

**JASMINE CHAITRAM**: Thank you so much, Nadia. I do have two questions showing for you right now. The first one is, how high are the liver enzyme values in order to be a concern?

**NADIA AYALA-LOPEZ**: Yes, thank you for the question. So one thing I want to note in these studies of COVID-19 severity versus patients who are not severe is that there's a lot of different cohorts that are included in these studies. And the way that these patients are subsetted were also different. So they may be comparing ICU versus non-ICU patients, or COVID-19 severe versus mild. And however they compare them is going to be different. So we would look at statistically significant changes versus clinically significant changes.

So as far as your question for the liver enzymes, it really depends on comorbidities that are present, any kind of liver function and liver dysfunction that is apparent, looking at different markers, such as albumin and bilirubin, as well, which I didn't talk about very much. But it's really taking the whole clinical picture into consideration for that particular patient. So I would not be able to give you a number, but it is clear that, in severe COVID versus non-severe COVID, that we are seeing some tissue injury. And that may be reflected in the liver enzyme markers if the liver becomes involved.

**JASMINE CHAITRAM**: OK, thank you. Our next question is, is there any data for patients with underlying conditions that may cause elevated liver enzymes, such as hepatitis or other autoimmune conditions?

**NADIA AYALA-LOPEZ**: I think this is a really good space where we need more information, because we do not have, that I'm aware of, that much granular data on these comorbidities and how they're associated with COVID-19 looking from the perspective of clinical laboratory abnormalities. I think we've done a really great job in managing these patients in the pandemic, and now is really the time to look at these studies that can be done really retrospectively.

So I'm sure others in the audience may have some more information on this. I did look into this. I think that we still need more information on how these comorbidities affect the markers, but also how informative are they, as well, and which markers can we rely on the most, depending on the comorbidities in that particular patient.

**JASMINE CHAITRAM**: OK. How frequently should we be monitoring these analytes? We are finding providers ordering these as daily labs, which is increasing in patient testing costs significantly.

**NADIA AYALA-LOPEZ**: Yes. It's a really great question because not only does it increase costs, but also resources. We're very limited on resources, and having to go out to the floors to draw each of the patients is really taxing on clinical laboratories, clinical laboratory staff, and phlebotomists. So utilization management in the setting of COVID-19 is extremely, extremely important.

And it really would also depend the what the status is of the patient and what interventions can be done in order to help their management. So there are different phases of COVID-19 that we're seeing, from the mild phase to more of an inflammatory or accelerated stage, and then in severe disease. So there really needs to be more studies to look at how quickly do these markers change in these different phases of COVID, how are they going to change and be informative during therapy, such as corticosteroids that are being administered, or antibody therapy, as well, to understand how frequently we need to monitor these markers. And also it depends on the marker, as well. So if they're on anti-coagulant therapy, that would necessitate, or at least suggest, monitoring of anti-coagulant therapy. And if they're not needed that anti-coagulant therapy, then monitoring would be less frequent.

So it really depends on the phase, I think, of the response-- or of COVID-19 that the patient is in, which is why it is important to know and have those diagnostic tools to understand the progression of their disease. And these predictive markers, such as the neutrophil to lymphocyte ratio, looking at D-dimer levels seem to be that window of opportunity to look into that further.

**JASMINE CHAITRAM**: Nadia, thank you so much for joining us today. I wasn't able to ask you all of the questions that are in the Q&A box, but if you want to look through them and respond to them online, I'm sure our participants would appreciate seeing some of those answers live through the Q&A box. And in the interest of time, unfortunately, I am going to have to move to our next speaker. So thank you again for taking the time to be with us today and presenting all this useful information.

**NADIA AYALA-LOPEZ**: Yes, thank you for the invitation.

**JASMINE CHAITRAM**: OK. Our next speaker is Chris Elkins. He's with the CDC COVID-19 Laboratory Testing and Task Force. He's actually currently the lead. And he's going to be talking

about COVID-19 barriers and surveillance. I know a lot of you have asked about what CDC is doing. And so you're about to find out.

**CHRIS ELKINS**: Thank you, Jasmine. And I appreciate the invitation to talk about SARS-CoV-2 variants, given the intense interest in them lately, but also how they're intrinsically linked to how CDC is looking at surveillance at a strain level across the nation. So we can go ahead and forward the slides.

So in essence, what we're going to do is give you an overview of our national SARS-CoV-2 strain surveillance system, referred to as NS3, give you a bit of an update on the SARS-CoV-2 variants of interest that we have been tracking, and then just a brief summary.

So the idea of looking at surveillance of SARS-CoV-2 at a national level really took shape back in the fall, and was initiated in November of this past year. The goals for this type of surveillance is to establish a representative system for baseline virus surveillance across the country. But importantly here is to build a high-quality collection of representative SARS-CoV-2 specimens and sequences. And these will be used, then, for isolation and characterization of the virus.

The strategy here involved our public health laboratories initially providing 600 specimens, approximately, to CDC every two weeks. That's being expanded to 1,500 specimens to CDC every two weeks. And it's very timely because that expansion starts as of today, the 25th. That expansion has also built upon somewhat of a population basis, where every two weeks, every jurisdiction should be sending a minimum of 10 specimens to CDC. But those numbers are based and scaled to a population base within each of those jurisdictions.

The specimens are intended to be coming from a variety of geographical locations over time. Demographic and clinical metadata will be contributed. And realistically, these will provide the viruses, reagents, and constructs for the US government, academic, and private developers. Next slide, please.

So this is a picture of what we have so far, noting, of course, that we started back in November, and then we're scaling up currently. So from November 2020 to the present, we've established a representative system. Most states and territories are participating. And a little over 1,100 specimens have been sequenced to date. And again, expanded to 1,500 specimens to CDC every two weeks.

So what are we really looking for here in our selection criteria? Of course, number one is looking at those diagnostic specimens that are coming in from molecular platforms that have fairly low Ct value. So we're asking for specimens that are less than or equal to a Ct of 28. The original clinical specimen. And given what I've mentioned before about a collection of specimens for downstream characterization, we of course wanted them collected in media that allows for viral culture. So we're not looking for specimens that are collected in things like molecular transport media.

Again, the samples representing our geographic, demographic, but as well as clinical diversity. And specimens collected in a timely way, so wanting to have those that are collected within the last two weeks for each collection period. And that will allow us to get a general assessment, a temporal assessment of specimens and their diversity as it's changing over time.

In this regard, I think that having that collection is going to be very fundamental to then pursuing what we're looking for in terms of the variant issue. And it allows us to say more generally, with the wealth of genome sequencing data that's being crowdsourced across the world, and of course across the country, how representative our collection is, and can compare it to those larger data sets. Next slide, please.

So another piece of enhancing the surveillance for SARS-CoV-2 is also expanding our commercial laboratory support. And this is involving new and expanded sequencing contracts through the CDC. Currently, we had contracts with Illumina and LabCorp, but we're also bringing on a Quest contract that's really increasing our sequencing prowess from 2,500 sequences generated per week to approximately 6,000.

And there are some specific biases that we will be able to have flexibility to employ, going after certain variants, such as those variants that can be detected on the Taqpath platform, looking for the S gene target failures. And that's something we'll get into in just a second. But this does allow enhanced flexibility and enhanced coverage across the United States. Next slide, please.

So when we dive into the variant issue, what variants do we consider of interest? Certainly, the B117 lineage that emerged in the UK in September of 2020, but has become prominent back in December. This is, of course, found at this point in approximately 55 countries, including US and Canada. And it's characterized by a couple archetype mutations, namely the 501 mutation and others that are noted. But specifically, there's a deletion within part of the genome that produces an S gene dropout within the Thermo Fisher Taqpath instrument that I had mentioned just previously.

So there's a specific pattern there where the S gene is not detected, whereas ORF AB gene gene is, as well as N gene target. And so that allows a diagnostic platform to somewhat triage those samples that may be of interest for looking at the B117 variant. It's also important to note that not all deletions-- these deletions also exist in other strains, so not all deletions and the S gene target failure that may be observed with the Thermo Fisher platform are B117 lineage. So that's important, as well, to note in terms of what you're observing locally.

The second variant of interest is the B.1.351 lineage. This was first detected in South Africa in October of 2020, and is now in over 15 countries. And these involve multiple substitutions in the spike protein. Namely, again, the 501 mutation, and also 484, which is a significant mutation to track, as well, along with the 417 mutation.

These mutations, as the ones I mentioned before in the B117, are associated with the spike protein. And this is thought to be important in binding, and also in transmissibility of the

variant. And so these are, of course, those mutations that rise to the level of interest to be able to track. And there is some evidence to indicate that the 484 mutation may affect neutralization by antibodies.

Finally, there's the P.1 linage. This is a branch-off of a B.1.1.1-- I'm sorry, B.1.1.28 lineage. This was first reported by the National Institutes of Japan involving four travelers from Brazil. It contains 17 unique amino acid changes and three deletions.

Again, if you note that the mutations here of interest include 484 and 501. Interestingly, D614G mutation, which is a mutation we've seen here in the United States that has traveled across the country during the course of the pandemic from early spring and through the summer, and there may be additionally circulating in Brazil a lineage that occurs without the 417 or the 501. Next slide, please.

So what is CDC doing with regards to the known variants of interest that are circulating internationally? So we're enhancing and using the baseline broad surveillance strategy that we talked about in the last few slides, but also targeting those towards variants of SARS-CoV-2 and our expanded commercial laboratory support. So as I mentioned, being able to target some of these S gene target failures very specifically with some of our sequencing contracts, but then also allowing additional specimens to be sent to CDC with regards to these variants of interest.

So in addition to the biweekly shipment of baseline surveillance, we're also asking for weekly shipments for targeted surveillance through our public health counterparts. And these will have a more narrow selection criteria, and they will tend to be-- and rightfully so-- dynamic short-term requests that can be more nimble and able to be changed as necessary. So the guidance right now, as it's continuously being updated, is interested, of course, in the B117 lineage. And those are able to be triaged by those folks that have the Taqpath, but also given the FDA notification of the Linea system, which also has a target failure that may have a pattern that may be useful, would be good for being able to triage those samples and specimens for further study.

The B.1.351 linage, which at this point is primarily detected by sequencing, and of course some of our public health counterparts do have significant sequencing capacity, what we're asking for is being able to have those forwarded to us as they occur. And then, of course, future variant viruses, such as the P.1 variant.

So again, the commercial laboratories, their initial focus will prioritize these S gene target failures and help improve detection. But again, I will stress that not all S gene target failures are the B.1.1-- I mean dot seven variant. They may involve the target failure that has a deletion that occurs in other strains, as well. Next slide, please.

So where are we at in terms of the B.1.17 variant? The SARS-CoV-2 cases, as of January 24th, there are 22 states that have approximately 195 cases. And so this is how the national picture looks. And at this point, we have no confirmed cases of any of the other variants that I talked

about. And our focus here, of course, is understanding the nature in which these are expanding over time, noting a couple states with some significant cases, in terms of California and Florida, and understanding, of course, from an epidemiological perspective what these particular cases-- how they proceed and what types of trigger points we may want to look for in terms of signals of either increased transmissibility or mortality.

I will say one of the other things that CDC is working on is understanding and having and relaying a better basis for classifying variants. And if you noticed that I referred to them as variants of interest, that's how we refer to them in our guidance for enhanced surveillance and baseline surveillance. That's found on the APHL website. Because at this point, they are, of course, something that we're interested in tracking. And that's something that we're dedicated to do. Next slide, please.

So in summary, what we're trying to do here is develop a surveillance system that allows us to capture not only the genomic information that we can track over time, and understanding the prevalence of these various variants of SARS-CoV-2, but also obtain good, solid specimen and culture collections so that we can do the functional characterizations that are required to either enhance our concern and relay those appropriately. And so that involves cultures that we can understand better how diagnostic escape or failure can occur, how these viruses, once they're grown and propagated, react to neutralization by convalescent sera or from sera from folks that have been vaccinated, and of course understanding monoclonal therapies and how they are impacted by these mutations.

And so these are all very important endeavors that will require us to be able to grow up these cultures and do some of these functional studies, but as well provide these cultures as a resource to academia and other government counterparts. And we have been doing that, in terms of growing cultures to scale to be able to send to repositories such as BEI. So at this point, I'm happy to take any questions, and appreciate the time. Thank you.

**JASMINE CHAITRAM**: Chris, we appreciate your time, as well. There are a few questions. I'm going to ask you a few of them. I won't be able to get to all of them, based on the time we have left in the call. We still have two agenda items. But the first question is, "can you describe the evidence that 484 affects neutralization? Was this evidence generated or confirmed by CDC?"

**CHRIS ELKINS**: There is no evidence as of yet that's able to be confirmed by CDC. We have, of course, been able to obtain, or are in the process of obtaining some of these cultures from the international sources. And it does take some time to be able to get those in the agreements to be made and to be grown to any extent to generate functional assays.

So at this point, I can say no. There is some literature out there to suggest that, again, without-- and some of it is preprint-- that there may be some inability for convalescent sera to neutralize certain members of these variants. So that's something to be taken, of course, but we need a better body of evidence to have a good idea of what this will mean over the course of the population.

The other aspect, of course, is that some of the studies that have been done have been done with pseudoviruses, which are a little bit extrapolated from reality. But there is, of course, these are model systems, so it's important to understand their effect in a pseudovirus system versus in a real life situation, and understanding the biology that goes into that.

**JASMINE CHAITRAM**: Thanks, Chris. The next question is, "will the genome sequencing data be made available to the submitting laboratory?"

**CHRIS ELKINS**: Yes, it will be. It's intended to-- and all of this surveillance, the baseline surveillance and variant surveillance and so on, is intended to be returned back to the submitting laboratory, along with certain pieces of analysis.

**JASMINE CHAITRAM**: OK. And how should research laboratories that identify a variant of concern report these results to public health? These are research laboratories.

**CHRIS ELKINS**: I would suggest that they work through your public health laboratory so that the specimens can be obtained. And those public health counterparts, laboratory counterparts will be able to connect better into our streams for this type of surveillance activity.

**JASMINE CHAITRAM**: OK, great. And then I got two questions about a variant that is CA20C. Does that sound familiar?

**CHRIS ELKINS**: OK. Yes. That's a variant that was identified I think essentially about a week ago-- well, it was brought to our attention about a week ago-- based in California. And it involves a constellation of mutations, some of which we've talked about here, but also understanding that the particular mutations, I believe, were seen originally in July, and in this country, in California.

And then some of the academic sequencing counterparts have been monitoring the prevalence of this particular mutation over time, and has seen an increase in specimens that are positive for that particular variant from November and into December, increasing at a good rate. So that is something that we're looking into. And it's also important to note that the Department of Public Health in California certainly is aware of this, and I believe had a press release about this with more detail.

**JASMINE CHAITRAM**: Chris, that was a great presentation. Thank you so much for joining us today. We are going to move to our next speaker.

Our next speaker is Sarah Harding from the Centers for Medicare & Medicaid Services. She's been on this call before. We've asked her to come back to answer a few questions about billing. And I think she has a few questions queued up, and then we can ask her a few more, if any of you submitted them through the Q&A box. So Sarah?

**SARAH HARDING**: Yes. Thank you very much, and thank you for having me back again today. We have gotten a few questions that I will try to answer, and then can certainly take others.

Yes, thank you for putting these resources up. These are good links to be able to get information.

One question that came up on a previous call that I just wanted to touch on briefly had to do with the different payment rates from various MACs, which are the Medicare Administrative Contractors. And as we talked about before, unless CMS posts a national payment rate for any given test on the clinical lab fee schedule, the local carriers, the local Medicare carriers are responsible for setting those payment rates. And so CMS has only posted national payment rates for a handful of COVID-19 tests, and the rest of them are indeed covered and paid for by the local MACs.

So by the end of the day today, actually-- the timing was great for this call-- there will be a table posted online. This will be on the-- if you look on the CMS.gov page and look for the Current Emergencies, there's a huge amount of information related to COVID. But under the section called Billing and Coding Guidance is a fact sheet for payment information.

And that page, that sheet will be updated with the individual payment rates for COVID-19 tests. So you'll get a sense of what different carriers are paying. But certainly if there are other questions after that, I can certainly answer. But that was one topic that came up. I believe the fact sheet, in particular, is called Medicare Administrative Contractor COVID-19 Test Pricing. And so it will be posted with an update, again, either later today or early tomorrow.

OK, so we did have another question that had to do with pooled sampling, so the idea of running a batch of COVID samples and then rerunning if one of those came up as positive. At least, that's how we've been informed of the process. And whether that would be paid for by Medicare. As of today, the answer is no. There is at least no national coverage decision for pooled sampling.

There are a couple of sort of roadblocks that get put up specifically with pooled sampling, and that are really not covered under Medicare statute, particularly on the coverage side of things, which is not my expertise, but where pooled samples may be used, especially for surveillance, that is not going to have a benefit category under Medicare, typically. And then the other just kind of issue is, when it's in a pooled sample, not being able to attribute the test to a particular beneficiary. So even if you had a pooled sample of all Medicare beneficiaries, the test has to be done for a particular individual.

But as I said, that's as of today. We've certainly seen a lot of things change over the last year, so I don't know if that will be changing at all. But as of today, the answer is no, there is no national coverage policy for pooled samples.

Other questions that we've seen have had to do with anticipating some coding, some coding decisions. Those types of questions really are under the purview of the American Medical Association CPT Committee, which is the group that sets the codes that Medicare follows.

Although there have been a few codes that CMS has created, on a whole, we typically leave that to CPT, since those are the codes that all payers will use.

So to my knowledge, the codes that exist right now for COVID-19 testing are what are in place. But I know CPT has been working very hard to stay current on trying to create codes to make sure they are as up-to-date and describing as well as can be described each of the various tests and types of tests, vaccines, and whatnot. So I don't have a good answer for the questions that had to do with the specific coding options, except to say to continue to watch the AMA CPT language that does get published.

I believe that was it for the questions that I had gotten. There's a question here about uploading the direct link for the new reimbursement schedule. Yes, I believe I can at least get you to the Current Emergencies page. And then as I said, it is a fact sheet under the Billing and Coding Guidance section. I will put that link-- well, I'll put it in the chat and let--

**JASMINE CHAITRAM**: Yes, that'd be great.

**SARAH HARDING**: Perfect.

**JASMINE CHAITRAM**: Put it in the chat, please.

**SARAH HARDING**: So it's in the chat. And I don't want to put the link to the old fact sheet, just because that won't help you. But as I'm looking at it right now, it has not been updated. But I expect it to come up later tonight or first thing tomorrow.

**JASMINE CHAITRAM**: OK, and then if you could answer just one more question before we go to FDA's update, it just came in, it said, "did CMS issue guidance on the incentive payment for rapid results for COVID testing already?"

**SARAH HARDING**: So I believe-- oh, there's an echo coming. I believe that that guidance did get up. While the FDA is talking, I will go and find it and put up a link. If it's not published, it just means that it is in a very long and complex clearance process, which means it's coming, but I won't have good information on exactly when. But so give me a minute to go and get it. And if not, it is coming soon.

**JASMINE CHAITRAM**: OK, thank you, Sarah. There was another question, but you answered it when you were talking to us about billing, being able to bill for pooled samples. So thank you for covering that. And we do appreciate your time being on the call with us today and for putting those links in the chat. So if you've got anything else to share, please put it in the chat.

**SARAH HARDING**: Perfect. Thank you.

**JASMINE CHAITRAM**: Thanks. OK, we're going to our last agenda item for today. It's Tim Stenzel from the Food and Drug Administration. He is a standing item on our calls, but we did not do a sound check, so I hope it all goes well. Tim, are you there?

**TIM STENZEL**: Can you hear me, Jasmine? Can you hear me?

**JASMINE CHAITRAM**: Yeah.

**TIM STENZEL**: All right. And Dr. Sara Brenner is going to help me with one of the responses. So we have a number of questions that we received, and we have answers hopefully. The first question is, "any information about mutations affecting overall testing accuracy for molecular testing?"

So as we discussed in our letter to clinical laboratory staff and health care providers on January 8th, we are conducting ongoing assessments of the potential impact of known variants on associated molecular tests. I will say that those known variants, you know, we look at sequence databases, we look for anything that looks significant in terms of prevalence. There are literally so many mutations that to do this for every mutation may be difficult. And I'll get to that. So that's where we understand where variants of importance come from, or we understand the Brazilian, the South African, and the UK variants. We look into those.

At this time, we have identified three tests that may be impacted-- Mesa's Accula, Thermo Fisher's Taqpath, and Applied DNA Sciences' Linea. Linea and Taqpath have an S gene dropout. Otherwise, their performance is probably unchanged, unless there's other variants in the other targets, because they both are multi-target assays. Mesa's assay is single-target.

Based on available work that's now been put into their IFU their package insert, it does not look like there is a significant impact by the mutation that we described there. It's not the UK variant, and I'm blanking on the exact designation. I'll come back to that a little bit later if I can find that. So to date, we do not see significant impact. Specifically, we have no assays that are affected by, say, the N501Y mutation that's present in all three variants.

OK, moving on to the next question. "With respect to the Curative communication, the notice states to follow the IFU for false results. Is that not true of every EUA?" You are correct in that no assay test is perfect, and that performance can change if the IFU is not followed. However, in the case of Curative, there is additional unique language in the labeling when we authorized the test.

And we felt it was important to inform stakeholders of this who may not be aware. And specifically, the FDA does not recommend Curative assay be used for asymptomatic screening, that the oral swab negatives be confirmed by another sample type and/or test, and that also collection be observed in every case by health care workers. And Sara, if you're on, you're up next.

**SARA BRENNER**: OK, thank you, Tim. So we had a couple of questions related to at-home tests. The first was how widely available are at-home tests. The FDA doesn't track manufacturing data and distribution data, so unfortunately, we don't have specific numbers at this time with regards to how widely at-home tests are distributed. But what we can say is there are currently three tests that have been authorized for at-home use.

Two of those are by prescription, the Abbott BinaxNOW™, which is an antigen test for at-home use, again by prescription, and then the Lucira™, which is a molecular at-home by prescription test. And there's one nonprescription or over-the-counter antigen test. And that's Ellume's test. So there are three total used at home, with one of them being fully over-the-counter that have been authorized so far. So really, the availability has to do with the manufacturing capacities mostly of those three different developers and their distributions.

The second question was what are the reporting requirements, which is a question and an issue that we've talked about a lot on these calls, and in many other venues. From the FDA's perspective, the FDA doesn't have a federal legal requirement, but we're asking developers and all those involved to have a plan to allow for the reporting of results consistent with all other COVID tests that are used in laboratory and CLIA environments, for example. But as rapid testing increases greatly in the US, our federal and state response systems really need to have the most comprehensive diagnostic data available, which is critical for guiding public health responses at the local, state, and federal levels.

I'd also like to point out, and then I'll drop in the chat to all panelists-- I'm doing that now-- hopefully, you guys can see it, and Jasmine, feel free to disseminate however you like-- that last week, a detailed FAQ was released by HHS regarding reporting requirements for all COVID tests at the federal and state levels. And this is really an FAQ that pulls together information that's been provided by HHS over the last six to nine months regarding specific data elements, the harmonization and standardization, the specific technical specifications around how the data should be coded. And then it lays out in a single chart or a single table the federal and state reporting requirements by each data element that was listed in the June 4 guidance. And then it breaks apart, but puts side by side, the lab-based and non-lab-based tests.

So my hope is that, if you have further questions, you can check out that resource, and it will clarify and bring together some of the information that's been previously provided. That's it. And back to you, Tim.

**TIM STENZEL**: Thanks, Sara. So I'm going to circle back to the mutation topic, the first one. So the mutation that may affect the Mesa Biotec] is a 2883 GGG to ACC. So it is a three-base change. Three-base changes are potentially going to have a bigger impact, as are in dels, as well.

The other point to make about that is multiple target assays will be better. There can be very low-frequency mutations that can knock out a single gene, or a single-target assay. And multiple variants could knock out a multiple-target assay. So whenever you have a suspect

sample that seems like it should be positive, the recommendation is to test with another molecular assay.

The next question has to do with self-collection. With self-collection of nares and other respiratory sites used by the FDA EUA'd SARS-CoV-2 molecular tests, but have not been EUA for self-collected specimens render the nucleic acid test a lab-developed test. So I think adding self-collection to an assay is the question here about what the FDA thinks. So we have stated in our FAQs that on-site self-collection is appropriate for mid-turbinate anterior nares swabs-- not talking about saliva, oral fluid-- unless specifically prohibited in a test labeling. And that nasopharyngeal and oropharyngeal specimens are not appropriate for self-collection. Home collection, however, collections outside of permanent and/or temporary health care facilities, need to be specifically authorized.

And finally, the last question we had to prepare was, for the Abbott ID NOW, could it be affected by the UK variant. As noted in our safety communication discussed earlier, only three tests were mentioned, and none of them were the Abbott ID NOW. And that concludes the questions that we've received ahead of time. Thank you.

**JASMINE CHAITRAM**: Thank you, Tim. Really appreciate that. We did get a couple more questions today. I will have to send those to you later, though, because we are at the top of the hour and at the end of our call. So I do want to thank all of our speakers for joining us today, and for the great presentations. I want to thank all of you for being here with us and tuning in, and also submitting your questions. And please remember that our next call will be on February 8th at 3:00 PM. And if you're not receiving messages from CDC, you're welcome to send us a note at LOCS@cdc.gov. And I think that's it for today, so everybody stay safe.