This content was published before guidance to change "monkeypox" to "mpox" was delivered to CDC programs in December 2022

Agenda
Clinical Laboratory COVID-19 Response Call
Monday, July 18, 2022, at 3:00 PM ET

- **Welcome**
  - Sean Courtney, Division of Laboratory Systems, CDC
- **SARS-CoV-2 Variants Update**
  - Clinton Paden, Division of Viral Diseases, CDC
- **A System for Early Detection and Monitoring of COVID Variants**
  - Eric Lai, Rapid Acceleration of Diagnostics (RADx) Initiative, National Institutes of Health (NIH)
- **FDA Update**
  - Tim Stenzel, US Food and Drug Administration (FDA)
- **Monkeypox Update**

  Christina Hutson, Monkeypox Response, CDC

SEAN COURTNEY: All right. Good afternoon, everybody. And thank you for joining us today. My name is Sean Courtney. And I am a health scientist in the CDC's Division of Laboratory Systems. On the screen is the agenda for today's call, which you can see also includes some discussion around the current monkeypox outbreak. But before we get started, I want to cover a few announcements and some of our general housekeeping items.

So DLS is CDC's division that works to advance laboratory quality and safety, data, and biorepository science, and workforce competency. We also work closely with the clinical and public health laboratories across the country to support laboratory emergency preparedness and response activities and have been hosting these calls since March of 2020.

So DLS supports this work across four goal areas. So we have quality, workforce and training, preparedness and response, and data and informatics. And the first announcement, I'd like to mention today is that CDC has recently developed two new web pages on monkeypox guidance. So we have Laboratory Procedures and Biosafety Guidelines and a How to Report Test Results web pages. So we'd like to ask you to share these new resources and review them or just share them with your network and your colleagues.

We've also published the Clinical Laboratory Biosafety Gaps: Lessons Learned From Past Outbreaks Reveal a Path to a Safer Future. And that is currently available. This publication highlights the importance of biosafety in clinical laboratories and how it impacted the 2014 Ebola outbreak response.

Additionally, CDC's OneLab has developed a laboratory communications toolkit that helps laboratories develop plain language communication strategies as well as developing a sensitivity and specificity job aid that helps public and clinical laboratory professionals understand how specificity and sensitivity

performance characteristics affect test result interpretation. And so this job aid, as well as the lab communications toolkit on the previous slide, are both now available on the CDC OneLab web page.

In addition to that, the Next Generation Sequencing (NGS) Quality Initiative has updated their Tools and Resources web page. And excuse me. And this is available on the-- I think the link is being dropped into the chat. So that's going to be useful to support your laboratory's NGS Quality Management System needs. So you can take a look at that web page as well to learn some more.

And so lastly, one of our large announcements is also that we're going to be working on rebranding these calls. So currently, this has been the Clinical Laboratory COVID-19 Response Call, the CLCR Call. And we're going to be rebranding those over the next few weeks to now being LOCs Calls, or our Laboratory Outreach Communication System.

So these calls originated in response to the COVID-19 outbreak. However, the scope of these calls has since expanded to include topics other than COVID-19 such as the current monkeypox outbreak. And so we want to make sure that the topics discussed during these calls continue to remain useful and really relevant to the work that you all are performing in your labs.

And so with all this, we want to hear from you. Our Training and Workforce Development Branch is interested in learning about any education or training gaps that you all are seeing. And so if you have anything that you'd like to share, we would like to invite that feedback at labtrainingneeds@cdc.gov. And as always, the slides and transcripts and audio from today's call will be shared, hopefully by early next week. And they can be found here on our Preparedness Portal.

And during today's call, we'd like to ask you if you have a question to please use the Q&A button within your Zoom function and that, when you do that, if you could also please include your email address so that if we do not have time to get to your question during the call that we can kind of follow it up after the call and make sure that we can get that addressed. And as always, our slide decks may contain presentation material from panelists who are not affiliated with the CDC. And presentation content from external panelists may not necessarily reflect CDC'S official position on the topics covered.

And with that, it's my pleasure to introduce our first speaker. We have Clint Paden with the CDC's Division of Viral Diseases who will be providing an update on the SARS-CoV-2 variant circulation. And Clint, I will go ahead and stop sharing my screen so that I can hand it over to you so just one second please.

CLINT PADEN: Thanks, Sean.

SEAN COURTNEY: All right, Clint. You should be good to go.

CLINT PADEN: All right. Can you guys see that? We all right?

SEAN COURTNEY: Yes, sir.

CLINT PADEN: All right. Good afternoon, everybody. This is a view of the national variant proportions based on the CDC-generated data and tagged baseline sequencing contributed by state and local submitters. The proportions here are weighted by the number of PCR positive tests within a state. And these most recent two weeks here are now cast estimates of current circulating variants.

A general note on describing the variant. As everyone may be aware of, using the Pango lineage system continues to evolve. Many of these new lineages that have been designated in the past few weeks under BA.4 and BA.5 are based on local transmission trends and don't necessarily represent a change in the spike gene. And CDC will continue to aggregate similar to what we have here and continuing to highlight new sublineages on the COVID data track as they become significant to the US.

So looking at this graphic focusing on the week ending July 16, last week BA.5 continues to increase and now comprises about 77.9% of new cases. BA.4 is predicted to decrease to about 12.8%. And the now cast predicts it to have already reached its peak and be on the decrease. Other lineages comprise less than 10% of new cases. And these are also in decline.

And the only lineage that we see that has a positive growth rate right now is BA.5. All of the sublineages that I mentioned under BA.5 have an identical S gene profile, save for BA5.5, which has a key 76i change. And just to note that, besides these, CDC does continue to monitor other emerging variants, particularly those with confirmed changes in the spike, both locally and internationally.

So around the US, we see sort of the same trend right now. BA.5 has risen to dominance in all regions, ranging from 72.7% of new cases in region three to 80% in region two. And again, BA.4 and other variants continue to decrease in every region. And as I mentioned, these data are from CDC sources and also from the NCBI, GenBank, and GISAID repositories from submitters who have done surveillance sequencing and has labeled it as so as described in some APHO guidance that we put out previously. If there are questions on that, I'd be happy to answer that or questions on whatever else. But I'll hand it back to Sean for now. Thank you all.

SEAN COURTNEY: OK. Great. Thank you for that update, Clint. I will give just a second to see if we have any questions that come into the chat-- sorry --into the Q&A box. But if none pop up, I'd like to ask you if you could just at least stay on the call today and if any relevant questions do come in, you can at least address them within the Q&A box over there. And while we're waiting for that, I will get my screen pulled back up.

I do not see any other questions coming up so, yeah, just if you can hang out on the line, Clint, like I said, if any questions pop up, that would be great if you could take over those.

All right. So moving up to our next speaker, we have Eric Lai with NIH's RADx Initiative. Eric?

ERIC LAI: Thank you. So let me just introduce myself for 30 seconds. I've been with the NIH RADx team as lead since May of 2020. I'm also the scientific lead of the Rosalind Bioinformatics System that's sponsored by NIH and a co-lead of the Variant Task Force since January 2021. And I'm the scientific lead for the ROSA Project, which I'm going to present, and also the ITAP project since October 2021. Next slide, please.

So just to give a quick background on the different variants that appear and disappear in the US, as all of us know, the virus appeared around December of 2019. It came to the US. In the beginning, there was just a Wuhan strain. And then about June of 2020, we start to see the variant B1.2. And it got to about 40%. And then it got taken over by Alpha.

So Alpha, going back in time, was discovered in the UK in about September of 2021 and started appearing in the US in about December, January time frame of 2022. Oh. 2021. And the Variant Task Force was formed in January of 2021. And one point I would like to mention is that almost all of the variants that appear and sustain have been-- appeared ex-US and migrated in the US.

There are a number of variants that appear in the US or originate from the US, but none of them really stay around long enough to be over 20% or 30%. So there is actually an opportunity for the US to see the appearance of the new variants in ex-US countries and then keep track of them as they move into the US.

And as you can see from this plot, the duration of the first appearance of these variants in the US and the time it takes to take over, to over 80%, 90%, 100%, is getting shorter and shorter in that Delta started up here in the US in about April or so. And it gets to about three months later or Delta, and Omicron it took only about a month to take over. So the duration of the variants when it starts to appear in the US, and then appear in the US, and then taken over like the situation we have now where BA.5 is getting shorter and shorter. Next slide, please.

So in August of last year, during one of the NIH Variant Task Force meetings, the Variant Task Force was asked whether we can develop a highly sensitive and specific assay for COVID that can detect all of the COVID samples and not sensitive to variants. At that time, as you can see from the previous slide, there were a lot of different variants. They were about half a dozen variants in the US.

So we, in collaboration with the FDA, have to test almost every single EUA authorized test out there to understand whether any of the variants will affect the EUA test that's on the market. And it was a lot of work. So we were asked whether there are any assays that we can develop that will not be sensitive to variant. And the second aim that we were-- the second question that we were asked was can we develop a system that can monitor nonvariants and, at the same time, potentially identify new variants in a cause and time efficient manner to complement the CDC sequencing effort.

Now we were unique in a position to address these questions because NIH has funded the RADx with multiple infrastructure to address this. First, the Rosalind database has the complete GISAID data from

GISAID. It is one of two databases in the US with a complete GISAID data. So we can look at all of the sequences at the same time.

Secondly, the RADx has the COVID sample biobank. Right now we have about 300 different samples now that exist of heating activated live samples from all different collection matrix, UTM, saline, and all of the variant. And we have existing contracts that can order them from five different CLIA labs. So as soon as the variant appear to US, we've been able to identify them and order them to prepare pools, individual samples for the testing. And then, finally, we have five testing labs that cover pretty much the whole country. Not only can get the samples but also test out our assays that we're developing. So next slide.

After going through about, at that time, about six million sequences we've been able to identify three markers. Two of them were known. One of them is the CDC SC2 region in the N gene. The other one is the thermal assay in the nsp10 gene region. And then we also discover that the S gene mutation, D614G, which started in the B1.2 variant about a year and a half ago in June of 2020, it's occurred in almost 100% of the different variant lineages. It is a positive selection marker.

And we have tested over 1,000 random samples now with these markers. And if you use any two of these markers, you have a very high PPA. And the samples that were missed a lot of time is because sensitivity issues of the assay and not because of the samples do not have those markers. So we have been able to identify at least three markers that is consistent across all of the COVID samples and is variant agnostic. Then we developed a second panel of markers. At the beginning, we took 48 markers that covers all of the known variants at the time-- Alpha, Beta, Gamma, Lambda, Mu. You name it, we had it-- and developed the state markers in collaboration with Thermo Fisher and tested over 1,000 samples blindly and determined the performance of all of these variant panels.

And the next slide showed the performance of the varying panels with the different market set. So if we take all 48 markers, you can see that the PPA and the MPA is very high. And the 48 markers were developed with the aim to make sure that we have redundancy. And once we have the data, we try to reduce the number of markers required to identify all of the known variants.

And as you can see, we get pretty good PPA and MPA all the way down to 16 markers. And when you drop down to 12 markers, some of the variant lineages start to disappear because we're not covered. So this demonstrates that we can develop a set of markers that can identify the different variants in a very high PPA and efficiency.

But what about new variants? So we do a simulation to determine what it is approach can be used to monitor or give us a hint of what potentially new variants are coming up. So what we did was that if you take the 12 marker set and you take out the markers specific for delta, you will realize that the number of undetermined cause as we go from 48 markers down to 24, to 16, 12, and 8, the number of undetermined samples, meaning that samples that we cannot assign a variant call, increases. If we take the 12 marker set, take out the delta markers, and then go into assimilation-- next slide, please.

So with 12 markers, there's about 10% undetermined cause. If you go back to the database and using the 12 marker set minus the two delta markers so that, at that time, back in March of 2021, Delta has not appeared in the US.

And if we would have genotyped the samples using this 10 marker set, you will realize that on the left plot starting in April, the number of uncalled undetermined samples would have gone up. And by the second week of May, the percentage of samples would have gone past 10% if we have used the 10 marker set. And then it'd go up very quickly, the number of samples that we cannot assign a variant call.

That if you look into the appearance of delta in the US and then now back look into these samples that we cannot assign, those were the delta samples. So what that means is that if we had ROSA Project up and running back in April where we can assign the nine known variants, except delta, and genotype and monitor the samples that are happening in the US, you will have observed a dramatic increase of unknown samples starting in May.

And those samples, if we have sent them to sequencing, you will have realized that those samples were deltas. So this system of monitoring current known variants and keep it in a very low percentage, and when you see unknown samples coming up and direct those for sequencing, we have an efficient method to monitor potentially new unknown variants.

Now in order to make this successful, a genotyping platform, just a genotyping platform, will not make it work. It has to provide a whole system. So next slide, please. We have, in collaboration with Rosalind and the partners, Thermo Fisher and some of our CLIA labs, we have developed the ROSA tracker, which is a publicly available web page up in the top where we are keeping track of the percent of the different variants with genotyping in the same dashboard. We also provided the tracking of sequencing.

And as you can see that as far as the percent of the different variants, they are very consistent with what we see from the CDC. Right now the undetermined cause as of last week is under 1%, so as would be reported by the CDC. Almost everything that we see so far, BA.5, BA.4, or BA.2. And if we see anything that comes out as undetermined and greater than a few percent, we would direct those for sequencing. So that's what we are keeping track of the known variants and potentially new variants. Next slide, please.

Now I want to make sure that we all understand what we're trying to say. We are not proposing to use the ROSA genotyping method to replace next gen sequencing. What we are proposing is to use the genotyping to monitor known variants and focus the use of NGS for detection of new variants. This shows the comparison of genotyping versus next gen sequencing and the different metrics of the two methods. There are one very important difference between the two methods in that the genotyping methods can genotype samples all the way up to about CT32, 33-- it's about 10 copies per sample, whereas the next gene sequencing right now most of the cutoff is in the CT of 27. So we are able to genotype and cover almost 100% of the COVID samples. And because it's about a third to a quarter depending on the lab and definitely is faster and for a lot of the labs, especially the smaller labs, the markers are publicly available.

It's on a website. Anybody can order the four markers, and use a standard PCR method, and any one of the current reader, and can determine what variants that they have.

Now NIH has been very generous to fund this project. And we are in the process of applying for funding for the next year to continue one more year of monitoring the known variants. However-- next slide, please-- in order for this method and the whole system to be adapted, there are a lot of things that needs to happen. A simple just a method will not do it. It will require regulatory input so that potentially some company can take this and make it into a diagnostic assay.

We're going to need collaboration with CDC for any kind of lab adoption and CMS in order to get paid because it is not getting reimbursed nobody is going to use it. And the long-term implication is that we're going to have to implement some kind of proactive monitoring and potentially some kind of expert panels to review the marker, composition, and update the market set at the regular level similar to other vaccines or other virus expert panels in order to update the panel and keep it up to date and useful. I will stop there if there are any questions.

SEAN COURTNEY: All right. Thank you. I appreciate that conversation today. We do have one question. And I'm not quite sure if it's maybe relevant for your discussion or if maybe Clint needs to jump back on. Are there any emerging variants or subvariants internationally that are currently a cause of concern?

CLINT PADEN: Sure. I can take a stab at that first. Right now there are potential interesting spike changes that CDC is monitoring, nothing yet that is I would call a concern.

International data is a little bit difficult to ascertain clear signal from noise just based on the varying quality, regularity, and amount of data that comes out of different countries. So trying to normalize all of that makes it sometimes you get a misleading signal. And so we continue to watch for these things, in particular as they show up in the US and with the goal of trying to obtain either examples of those viruses or of the spikes to test in the laboratory for differential response to vaccine neutralization.

SEAN COURTNEY: OK. Great. Thank you for that, Clint. All right. Eric, I do not see any other questions currently. But again, questions may pop up as we go. If you see any that come up in that Q&A window, if you could just answer them, that would be very helpful. Otherwise, if others do have questions, again, please include your email so that we can get them answered at a later time.

All right. And thank you for that, Eric. And so next, please welcome Tim Stenzel with the US Food and Drug Administration. Tim?

TIM STENZEL: Thank you, Sean. This is Tim from the FDA. And I appreciate being able to share some updates from the FDA perspective on this call. First of all, I want to give a huge shout out to Eric Lai and the entire NIH RADx COVID Variant Task Force Team, a truly historic and extremely effective collaboration between NIH, Emory University, the FDA, and others. It is representative of numerous NIH academic and FDA COVID collaborations, including others that include the University of Massachusetts,

the Independent Test Assessment Program, otherwise called ITAP, which assesses over-the-counter antigen tests, and, of course, all of RADx. The FDA also, with regard to the last presentation by Eric, is very open to genotyping EUAs and, of course, tests for full authorization.

And then I wanted to move in to updates then. So covered a little bit in the last segment and with questions. The Omicron lineage is, to our understanding and thanks to the Variant Task Force, are not expected to have an impact on test accuracy. So the mutations involved with the major Omicron lineages are not, to our knowledge, impacting results other than the fact that, for Omicron, for most of the sublineages, we have seen a huge increase in the number and the percent of low positive samples, high CT, low positive samples. And those, of course, can be very challenging to all of the antigen tests.

We're watching BA.5 very closely because it may, in fact, behave differently. There are some reports that there may be fewer low positives. And some of the early data suggests that that may be the case. So we could see improved antigen test performance with BA.5. So stay tuned. Really too early to make that definitive at this point.

I wanted to move on to some brief monkeypox updates. And first of all, I want to reiterate that the FDA continues to use enforcement discretion for LDTs as it has from the very beginning of the monkeypox outbreak. And also the FDA continues to assist the CDC in increasing a number of things. We have done a lot already together but wants to continue to assist the CDC in whatever will help expand access. And this has included increasing throughput in the LRN labs, allowing labs to report out results as positive instead of presumed positive-- since the CDC assay is a non-variola orthopox assay, not a monkeypox specific assay, that's FDA cleared-- and to allow reporting out as detected and not detected. That was a request which FDA was happy to oblige.

In many cases, we're providing enforcement discretion so that immediate alterations to the cleared assay can be made while we work through to codify those that we can codify. And then expanding the cleared assay into some national reference labs, which has resulted already in greatly expanding access and throughput and to help drive down turnaround times for tests.

Finally, perhaps many of you already noticed the FDA issued a monkeypox safety communication on Friday. The CDC sent a lab advisory with information regarding this out as well. The FDA does recommend that lesion swabs be used for diagnostic testing. The understanding of the performance of other sample types is not well understood at this time.

And so if a patient tests negative for diagnosis with a nontraditional sample type, including things like blood, urine, oropharyngeal swabs, and saliva - when they're not lesion swabs, we do ask clinicians and labs to consider retesting with a lesion swab if a diagnostic test result is important for that particular patient. And that ends the FDA updates for today. I'll hang on in case there are any questions. Thank you.

SEAN COURTNEY: All right. Thanks for that update, Tim. Really appreciate it. There was one question that kind of came through. And I feel like you could just clear it up pretty quickly. And it was somebody was asking if there were EUAs available for monkeypox testing.

TIM STENZEL: Yes. I can handle that. An emergency has not been declared under the Food, Drug, and Cosmetic Act invoking the 564 statute. And so there are no EUAs for monkeypox at this time. That obviously could change. But at the moment, we're monitoring this very closely.

And as I said earlier, were lab developed tests used without even so much as notifying FDA, although I think the CDC and the FDA would love to hear from labs who developed LDTs and have launched them. Again, that's not required. And then also working, of course, as I said, closely with the CDC to expand testing using the FDA-cleared CDC assay. Thank you.

SEAN COURTNEY: OK. Great. Thanks for that. Another question is, do we have any commercial tests available?

TIM STENZEL: So there are no other cleared monkeypox assays other than the CDC non-variola orthopox assay. The FDA is open to this but there being so few samples, validating a full authorization could be a ways off. But the FDA is totally open to this and monitoring this situation. And has reached out to many-- to some, I should say-- to some manufacturers where the FDA knows that they've developed tests to stay in close communication and offer assistance as they may need.

SEAN COURTNEY: OK. Great. Thank you. I think there are some other questions but I think they're more directed to CDC so I'll probably direct those to Christy after she gives hers. So I really appreciate you joining us for the call today, Tim. If any additional ones pop up, if you can answer those within the Q&A button. Otherwise we can get them handled by email later. So thank you for your participation today, Tim. OK.

And next we have Christy Hutson, who is with the CDC's Monkeypox Outbreak Response Team. So Christy.

CHRISTINA HUTSON: Hello. Good afternoon. Can you hear me OK, Sean?

SEAN COURTNEY: Yes, I can.

CHRISTINA HUTSON: Great. All right. Thank you for the slides. So today I'm just going to give an update of the monkeypox outbreak and some of the work we're doing for testing capacity, which Tim gave a nice overview of, as well as some of the testing that we do within the pox lab at CDC. Next slide. Go ahead move on. Thank you. OK.

So on the CDC web page, there's a nice overview of the outbreak summary. So I just pulled this information. This was as of July 15. And so at that time within the United States, we have 1,814 cases

within the country. And if you go to this page and click on that link, it actually shows a nice overview of each state and how many cases per state. Next slide.

Also on that page is a global overview, so again showing this nice map where you see the case breakdown by country. And on the right, we see the total, which is 12,556 cases. And then if you look at the different countries, Spain has the highest number at 2,835 followed by Germany, UK, and then the United States. Next slide.

So we've relied heavily from the start of this outbreak on our Laboratory Response Network. Through the past 20 years, CDC, in collaboration with other government partners, has worked to get FDA clearance on several diagnostic assays in the event there were ever a smallpox outbreak. So currently within LRN labs, we have an orthopox generic, which is not yet FDA cleared, our non-variola orthopox assay, and then two variola-specific assays. And variola is the causative agent of smallpox for those who are not aware.

So these labs are throughout the country. Some of you may be aware of them. They're basically there to poise the United States in case there was a biological terrorism event, which is why we already had a non-variola orthopox assay FDA cleared within that network of labs. Next slide.

Also on our monkeypox web page, you can go to this testing and case confirmation. And it just talks a little bit more about what we're doing, both within our LRN labs as well as how we are expanding to commercial labs. And so we've worked to-- yes. This is supposed to be Sean's [screen] so it should say testing and case conformation is what you should be seeing right now. These are my slides.

So CDC has worked with the FDA to move the non-variola orthopox test that is FDA cleared into these commercial labs. We now have it in four different labs. Sonic announced today that they were beginning to test with that FDA-cleared assay. And then at CDC, we're able to do specific monkeypox characterization testing of specimens that test positive for orthopox virus. Next slide.

These are the assays that we use at CDC under our CLIA approval. So we also use a non-variola orthopox assay. We posted the protocol on the CDC web page so that if anyone was interested in developing a lab developed test, they would have the primer and probes so they could develop that. Additionally, we also use monkeypox virus assays. This is based on some of our previous publications which we linked those also on the web page. Next slide.

And then we give specifics on our web page for the monkeypox assays. So we use a monkeypox generic assay within our lab, which shows-- it detects, sorry, the G2R, which is the TNF receptor gene. And then we also use within our lab a West African specific assay and a Congo Basin specific assay. And again, some of this information is up on the monkeypox web page, including a CDC SOP for the non-variola orthopox tests. And I believe our monkeypox generic SOP is also up on the web page now. Next slide.

We also within CDC do sequencing efforts. So this is actually an image from one of the earlier sequencing trees, just showing that in green the Portugal sequences, how similar they are to our red sequences. So early on, we recognized that most of these sequences were very closely related to those in Europe, suggesting that all these cases are likely part of one predominant strain. We recently did have a pre-press, so this multiple lineage of monkeypox virus in the United States, to detail some of these findings and some of these unique viral changes in the 2022 monkeypox isolates.

We saw in this analysis that most of these virus changes appear to be caused by an immune system protein called APOBEC3. And these APOBEC3-like mutations have been found throughout the monkeypox viruses since around 2017. But when you look at older isolates from both West Africa as well as Central African lineages, you don't see those APOBEC3 changes. We don't know yet if this is going to affect biological properties of the virus. And we'll need to do additional studies to determine if that's the case or not. And just important to note we're continuing to sequence isolates. And this information could change as we get more data.

And then the other paper I have at the top is one from our collaborators with Nigeria that details an outbreak within Nigeria. And it's interesting to look at that. Next slide.

I wanted to highlight some of the other work we do at CDC to try to understand this outbreak. So we do offer a pox virus serology assay. We have an IgG and an IgM assay approved under CLIA. So there are clinicians who want to submit serology to understand a particular clinical case.

And then we also do some different special studies. So for those who aren't aware, tecovirimat is the medical countermeasure that's used in some of these more ill cases. And so we're monitoring the target of that medical countermeasure, and if there are any genetic changes, then we do sensitivity testing within our lab just to make sure that those isolates with changes in F13L remain sensitive to the medical countermeasure.

We're also doing some different surveillance studies to try to understand if this virus was circulating before the first case was identified. So those studies have started. And we've started screening both residual nucleic acid as well as we're starting to get in some banked serology samples. So hopefully that will give us a lot more information. And additionally, we're doing some serology surveys at different clinics in a couple of different cities in the country to understand if the prevalence is higher than what we typically are aware of.

And then finally, we have received IRB approval to screen some different specimens under surveillance. So that would not be under CLIA. We cannot report those results back to the clinician or the patient but, to Tim's point, just understanding is there another specimen besides lesion, which we know is a very accurate specimen. Can we get data to verify another specimen type that might be appropriate for testing for monkeypox? Next slide. And that's all. I'm happy to take questions.

SEAN COURTNEY: Great. Thank you so much for that update, Christy. There are a few questions in the chat. And I'll just read some of them out to you. The first one is can VTM and/or UTM be used for the CDC monkeypox assay?

CHRISTINA HUTSON: Right. So we are very restricted, like many labs, by what our CLIA approval allows. We had to do some pretty extensive stability studies to show how long we could store specimens and that specimens within viral transport media were acceptable and did not cause inhibition. So our CLIA director has said we can test under our swabs in VTM based on that data. We don't have the data yet for UTM. And because there are some differences in the components of VTM versus UTM, we currently do not have approval.

However, it's really important to remember that LRN labs differ from CDC as far as which specimens they can test, again based on their CLIA approval. Same for the commercial labs. So it certainly is appropriate for a clinician to send a swab in UTM to the LRN or commercial lab if they're able to receive a swab in UTM based on the orthopox result because there are no other circulating orthopox viruses within North America. You can do contact tracing, isolation, requests of medical countermeasures, et cetera. So we do understand this is an inconvenience. And we really apologize for that. But at this time, CDC is restricted to dry swabs, swabs in VTM, and then lesion crusts.

SEAN COURTNEY: Excellent. Thank you for that response. The next question is, can labs request samples from the CDC for validation?

CHRISTINA HUTSON: So we try to work with the labs first. We've actually deposited monkey pox isolate, both our 2003 and then the newer isolates from this outbreak, with BEI. So we try to encourage labs to go there to make contrived clinical specimens. If there's a particular situation where they need clinical specimens, sometimes they can work with their public health lab or they can reach out to CDC. But we first try to do the contrived clinical specimens if that's possible.

SEAN COURTNEY: Great. Thank you. Next question is what are the testing protocols for BSL2 labs with no staff who are vaccinated for monkeypox?

CHRISTINA HUTSON: So on our web page, we put some specific biosafety guidance. And for labs that have BSL-2, if they're just doing diagnostic specimen processing and testing, there's some really specific guidance there about what we suggest for non-vaccinated staff, which is basically you would use BSL-3 procedures. And we list out some of those specific procedures in case you're not familiar with them. We also give information about once the nucleic acid is extracted from that specimen, then it's no longer infectious so then you can work with it out on the bench. But that information is up on our laboratory biosafety page under the monkeypox response.

SEAN COURTNEY: OK. Thank you. Next question is if non-variola orthopox is positive in swabs from multiple lesions on a patient, does CDC want the second swab from each lesion or just one per patient?

CHRISTINA HUTSON: We are happy to take whatever the lab prefers to send us. Generally, when they send us two, we test one. If it's positive, we don't go back. But if it's negative for some reason because it wasn't swabbed vigorously enough, then we would have that second one to fall back on. But in general, if you get a positive result at your lab, then just sending us the duplicate from that same lesion is sufficient.

SEAN COURTNEY: That's helpful. Thank you. Next question is does a commercial lab need approval to perform the FDA cleared test for the orthopox monkeypox test?

CHRISTINA HUTSON: So I'm happy to let Tim weigh in on this, but we work closely with these commercial labs to transfer the test over. We wanted to ensure that biosafety and training were sufficient. We worked with them very closely. We made sure that they were able to do necessary verification studies, et cetera. So right now, we're just focused on those labs that we've transferred the assay over to. Tim, I don't know if you have anything else to say about that.

TIM STENZEL: Yeah. No. Nothing else. We're working very closely with the CDC to just follow direction on how--

SEAN COURTNEY: Sorry, Tim. It seems like we're losing you. You have a bad connection here.

TIM STENZEL: Can you hear me now?

SEAN COURTNEY: A little bit. Go try again. Yeah. We'll give it a shot.

TIM STENZEL: I will try it again. So we're just supporting the CDC any way we can. So we're looking to the CDC just to see what they need. And the FDA will work very closely with them on any updates that are needed to be a cleared assay.

SEAN COURTNEY: OK. Great. Thank you, Tim. Next question is, Christy, what are the specimen storage guidelines for the real time PCR testing?

CHRISTINA HUTSON: So they're going to vary depending on, again, the CLIA approval of each lab. And I can put in there what-- I'm not sure if you're asking specifically about CDC storage. I can put that wording though in the chat so that you have it. I'm assuming that's what you're asking about.

SEAN COURTNEY: Yeah. That'd be helpful. Thank you.

CHRISTINA HUTSON: Sure.

SEAN COURTNEY: All right. And let's go to another question here. What specific extraction method is used with the CDC test?

CHRISTINA HUTSON: Right now we have a manual extraction, which is what was originally approved for this assay. And then we added the EZ1 extraction platform, which is an automated but small scale. We've been working with these commercial labs to add MP96, which we have enforcement discretion from the FDA for them to use. So that's what Labcorp is currently using. And I believe there's some other automated extraction platforms that we might be onboarding but those are the three right now.

SEAN COURTNEY: OK. I'll do one more question since we're getting low on time here. And that is so does the CDC need to receive samples from commercial labs for positive confirmation?

CHRISTINA HUTSON: Right now we are receiving the positive specimens or the specimens from the commercial labs. This is, in part, to monitor the assay performance as it's moved into these new labs. We're actually discussing internally, now that the outbreak has higher numbers throughout the country, if we can reduce the number that are being submitted to us to ease the burden especially on the states. But for the time being, yes, the commercial labs are also sending us all of the orthopox-positive specimens for characterization testing.

SEAN COURTNEY: All right. Thank you for that. And thank you for your participation on the call today, Christy. We really appreciate that as always.

CHRISTINA HUTSON: Thanks, Sean.

SEAN COURTNEY: And so with that, I just want to really thank all of our speakers today. As a reminder, this call occurs on the third Monday of each month from 3:00 to 4:00 PM. And our next call will be on Monday, August 15. As we've mentioned before earlier in the call, we'll post today's call on the website hopefully by early next week, so you'll be able to find the slides, transcript, as well as audio from the call. And with that, I just want to really, again, thank everybody for joining us today. And we continue to be grateful for all the work that you all are doing in your lab. So thanks. And have a great day.