Agenda
Laboratory Outreach Communication System (LOCS) Call
Monday, September 19, 2022, at 3:00 PM EDT

- **Welcome**
  - Sean Courtney, Division of Laboratory Systems, CDC
- **Monkeypox Update**
  - Serena Carroll, Monkeypox Response, CDC
- **Monkeypox Virus Sequencing in the 2022 Outbreak Reveals Multiple Independent Lineages and Unique Mutational Signatures**
  - Crystal Gigante, Division of High-Consequence Pathogens and Pathology, CDC
- **National Wastewater Surveillance System (NWSS): Opportunities and Challenges for Wastewater Surveillance for Monkeypox**
  - Carly Adams, Division of Foodborne, Waterborne, and Environmental Diseases, CDC
- **FDA Update**
  - Tim Stenzel, US Food and Drug Administration (FDA)

SEAN COURTNEY: All right. It's about two after three, so we'll go ahead and get started. So good afternoon, everybody. Thank you for joining us today. My name is Sean Courtney, and I'm a Health Scientist in CDC's Division of Laboratory Systems. On the screen is the agenda for today's call. But before we get started, I want to cover a few announcements, as well as some housekeeping items.

All right, so as you may have heard on previous calls, DLS is the CDC division that works to advance laboratory quality and safety, data and biorepository science, and workforce competency. We work closely with 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.

DLS supports this work across four goal areas. Quality, workforce and training, preparedness and response, and informatics and data science. As always, we'll be sharing slides from today's call, along with audio and transcript and we'll post them online by next week. You can find them on CDC's Laboratory Outreach Communication Systems page at the link shown here.

And so we continue to schedule these calls for one hour on the third Monday of each month. The next call is scheduled-- I'm sorry, I'm on the wrong slide. So sorry about that. So sorry, let's rewind that. Our Training and Workforce Development Branch would like to hear from you, so we'd like to hear any of your education and training gaps that you're currently experiencing. And so we invite you to send your feedback via email to labtrainingneeds@cdc.gov.

And during today's call, if you have a question, we'd like to ask that you please use the Q&A button within the Zoom system, and not the chat button. And also when you submit questions, to please also include your email address so that we can reach out to you if we're unable to address your questions during today's call.

And so with that, I'd like to remind you that these slide decks may contain presentation material from panelists who are not affiliated with CDC, and presentation content from external panelists may not necessarily reflect CDC's official position on the topics covered. And with that, I'm going to turn it over to Serena Carroll, who's going to provide an update on the Monkeypox Response. Serena?

SERENA CARROLL: Great. Thanks Sean, and thanks everyone. For those of you who don't know me, I am Serena Carroll, and I am taking over the Laboratory and Testing Task Force as the lead while Christy Hutson gets some much-needed rest and relaxation. I'm going to try and keep my updates short today so that we can hear from both Crystal and Rachel on some important sequencing and wastewater updates.

So just to recap, as of Friday afternoon, September 16, there were a total of 23,499 confirmed monkeypox or orthopoxvirus cases in the US. And this includes one US death that has been reported. There have been 869 new cases since the last reporting period.

A total of 99,783 specimens have been tested as of Wednesday, September 14, and the cumulative positivity rate is at 28.9%. Over 92% of our existing capacity still remains available within the US. And I don't have slides, I'm just talking through this, so thanks.

The CDC team completed sequencing for 200 monkeypox specimens this past week. And with that, I'm going to give a quick update on the LOCS message on the TNF receptor gene deletion. And then Crystal may have more to add when she goes into her presentation.

So as you all are aware, as of the September 2 LOCS message, CDC is aware of a small number of monkeypox cases in which preliminary data shows an approximately 600 base pair deletion in the Tumor Necrosis Factor, or TNF receptor gene. This deletion appears to be rare, but as many of you know, this gene is the target for both the CDC West African monkeypox assay, as well as the generic monkeypox real time PCR assay.

And LDT is designed using CDC's published primers and probes, specifically targeting monkeypox virus did not detect the virus because of the TNF receptor gene deletion. But because these samples were also tested with an LDT, based on CDC's published non-virulent orthopoxvirus test, these cases were still correctly diagnosed.

So in terms of preventing false negative results, we just wanted to stress that if your lab is using a monkeypox-specific laboratory developed test, please refer any highly suspicious monkeypox virus negative results to your public health laboratory, or to CDC to confirm results.

The public health laboratories and select commercial laboratories use the CDC, FDA cleared non-variola orthopoxvirus test which can correctly identify orthopoxviruses when the TNF gene deletion occurs. You may also want to consider using a multiplex assay that targets multiple viral genes, or an assay that targets an essential viral gene that's unlikely to mutate, or an assay that can detect non-variola orthopoxvirus.

So please let me know if you have any questions about that, and Crystal may have additional information as part of her presentation. Thanks.

SEAN COURTNEY: All right, Serena. Thank you for that update today. There is at least one question here, and it is, are those numbers indicative of an increase or decrease in the rate of new infections?

SERENA CARROLL: Is that in terms of cases overall?

SEAN COURTNEY: That would be my assumption.

SERENA CARROLL: So I think we've seen a decrease in overall testing recently, but there was a slight uptick in the number of cases that were positive last week. So I think we'll have to wait and see what the trends are, but that seems to be where we're at right now.

SEAN COURTNEY: OK, great. Thank you. There were a couple of other questions, but I think I'm going to wait for Crystal to provide her presentation because they may be more relevant for her to take-- to be able to answer. So if there's no more questions, Serena, I really appreciate your joining us today.
And if you're able, if you could hang around and answer any other questions that maybe pop up in the chat, we would appreciate-- or in the Q&A function, we would appreciate that. Otherwise, thank you for your participation today.

SERENA CARROLL: Thanks, Sean.

SEAN COURTNEY: All right. And with that, we're going to move right into our next presenter. We have Crystal Gigante, and she is from the CDC's Division of High-Consequence Pathogens and Pathology. Crystal, go ahead.

CRYSTAL GIGANTE: All right, thank you. I apologize up front. I'm a little bit sick right now. So please bear with me as I go through the slides some, and sorry for my voice. So I was just going to go through some of the observations we've had throughout this outbreak, looking at monkeypox virus sequencing in the US. Next slide.

Just as a little bit of background, in 2017, the largest outbreak of monkeypox in Western Africa occurred in Nigeria after decades of no identified cases. From 2018 to 2021, eight cases were imported to non-endemic countries from Nigeria. And since the re-emergence of monkeypox in Nigeria in 2017, there have only been two reported events of person to person spread of monkeypox outside of Africa.
That was until May of 2022 where this pattern changed, and we have many countries reporting monkeypox among persons who had no travel to monkeypox endemic countries. Next slide.

So far during this outbreak, all of the monkeypox genomes have belonged to Clade IIB, which was formerly called a West African clade of monkeypox virus. And the genomes published during the 2022 outbreak share a common ancestor with monkeypox virus from Nigeria. Next slide.

So the monkeypox virus genome is much larger than influenza or SARS-CoV-2. It's about 200 KB, double stranded DNA genome and contains about 200 genes. And this figure just shows a single monkeypox genome, which is not fragmented in any way, just going from the left end to the right end over four different lines.

And in the center of the genome, they've colored the genes blue based on their conservation level being very high across different orthopoxviruses. And the ends of the genome, you can see these coding sequences, or genes, that are red and yellow and green, indicating that they're less conserved. And many of these genes are either not present in some orthopoxviruses or are not very well conserved. These genes are typically involved in virulence, host range, or unknown function whereas those blue jeans in the center genome are typically essential genes. Next slide.

So our sequencing approach at CDC is sequencing DNA extracted from a lesion swab for PCR testing. The total DNA is very low off of these swabs, and the monkeypox virus DNA is somewhere between 0.1 to 5% of the total DNA. We do some screening where we only sequence samples that have a strong monkeypox virus positive PCR with-- and then we do a secondary screening once we have the sequencing data for an average coverage greater than 35.

We do a metagenomic sequencing approach using the details that are on the slide. I'm not going to go into too many details for this crowd. Next slide.

So thus far, we've identified-- and others-- two major lineages of monkeypox virus during the 2022 outbreak, and both lineages have been found in the US. Most of the samples fall into a lineage which has been named B1, which contain most of the US sequences and then also most of the global sequences. And that's shown collapse in the red triangle at the top of the phylogenetic tree.

The second lineage is A2, and so far there have been four 2022 US cases-- or three 2022 US cases and one 2021 case. It's also been reported in the UK, India, and Thailand and most of those cases have had traveled to Western Africa or the Middle East. And notably, there have been less reported person to person spread of this lineage A2 so far. Next slide.

So we had noticed, as well as others, that there were increased mutations in 2022 monkeypox virus, and that these mutations were specifically GA to AA mutations, which is indicative of a host antiviral protein called APOBEC3. APOBEC3 proteins, as I said, are part of the vertebrate innate immune system that work to mutate the virus and restrict replication.

What I can show on this figure here is a monkeypox genome spread across the line with all of the mutations in a certain clade or group or lineage, as these little vertical tick marks. And in blue tick marks are APOBEC signature mutations, and then red and gray are non-APOBEC.

And I hope you can see that Clade I, which is formally called Congo basin, and Clade IIA, which is a non-Nigerian monkeypox, West African monkeypox. Most of the mutations are red and gray, whereas the current outbreak, most of the mutations have been this blue APOBEC mutation. So it does look like a change in the way the virus has been mutating recently for this lineage. Next slide.

And another observation that we've had is some large deletions and translocations, or rearrangements, in monkeypox genomes. There's just a graphic of a few of these on the bottom. We've observed this sort of deletions in about 3% of the monkeypox genomes from the US.

And these deletions have the potential to impact diagnosis or efficacy of therapeutics because they are deleting, in some cases, dozens of genes. These are more common in the terminal regions of the genome, where non-essential genes are located.

And I have a red arrow here pointing to the J2R, J2L, CrmB TNF receptor gene, which is the one that has been mutated relating to that LOCS message. So you can see in this Florida 52 sample at the bottom, there was a deletion that deleted this-- that gene, as well as others.

However, in this monkeypox virus, because this gene is present in two copies, the other copy was actually intact. So it didn't affect the diagnosis for this case. For the case relating to the lox message, the mutation is much smaller, only 600 base pairs compared to this deletion, which is about 15 KB and it's just within the J2R gene and it is in both copies of the gene which causes the issue for diagnosis. Next slide.

So to summarize, we've found multiple lineages of monkeypox in the US in 2021 and 2022. Monkeypox virus sequences since 2017 have exhibited evidence of potential hosts antiviral editing mutations, and we've seen about 3% of monkeypox virus genomes contain large deletions or rearrangements.

And we have seen some of these deletions showing up in known contacts of the person, but not in every case. And continued analyses are expected to provide us more detail here. And there are so many people that have contributed to providing these samples, so you can go to the next slide and there's a list of some of the labs involved in directly the data that I showed.

But basically every lab is contributing samples to us, contributes to this sort of surveillance. So thank you all. And happy to take questions.

SEAN COURTNEY: All right, thank you for that, Crystal. I really appreciate that update today. There are a few questions that I want to go over. Not sure if they're going to be specifically relevant to you, but I'll still put them out there and if you can answer them, we'd appreciate that.

So the first one is whether the accession number for the TNF deletion-- for the variant-- is posted on the website.

CRYSTAL GIGANTE: Yes. So we're hoping to get that sequence out this week or get a sequence out this week. This mutation was identified in a public health lab, so we're trying to get our sequence out there so we can provide that accession number as soon as possible and then share that for others to see.

SEAN COURTNEY: Great, thank you. The next question, you kind of covered this actually in your talk today but I'll ask again. It was, can you tell us where the deletion is? Was that in the forward, reverse, and probe, for example?

CRYSTAL GIGANTE: Yes, so it's a very large deletion and so it actually deletes the target region for both assays, the West African or Clade II-specific, as well as the monkeypox generic. So they're both affected by this large deletion, 600 base pairs.

SEAN COURTNEY: Great, thanks for the clarification. Next question was, is there a difference in clinical presentation between the two lineages that you mentioned?

CRYSTAL GIGANTE: So there have been reported differences in clinical presentation between the Clade I and Clade II monkeypox, or the West African and Congo basin. But there have been so few cases if the person is talking about between the B1 and A2. There have been so few cases of the A2, I don't think anyone's done that analysis yet.

But as far as we can tell, there haven't been any deaths-- or there haven't been many more deaths associated with one versus the other. But as I said, there's only been a handful of cases of A2, so I think that's kind of like an ongoing investigation to see if there are anything clinically distinct about those two.

SEAN COURTNEY: All right, thank you. Next question is, is there any evidence that one or more of these monkeypox genome mutations have-- has been associated with an increase in the transmissibility of the virus to humans?

CRYSTAL GIGANTE: No. Again, that's like an active-- something that many people are looking into. So what we'd have to do is get the virus into culture and see how well these viruses grow. We don't have evidence right now of that occurring. The viruses that I showed that we identified at CDC, they weren't associated with further transmission outside of the cases that were identified. And that's kind of all I can say about that. But yes, it's definitely something we're looking into, and others are looking into.

SEAN COURTNEY: Thank you. Next question was, what is the percentage of the cases that are sequenced?

CRYSTAL GIGANTE: That's a little bit harder to come at right now. So we do attempt sequencing on most of the strong positive samples, but then we have kind of a quality threshold for which we put-- we publish and make publicly available. So it really depends.

We do hope eventually to sequence all of the samples that have a reasonable amount of viral load and get that data available. But we imagine some of those will require some enrichment, possibly culture. So they've kind of been put aside until we have the resources to focus on that troubleshooting step.

SEAN COURTNEY: Great, thank you. And then I'm going to ask one last question that kind of follows up on that. And that is like out of the cases that we're receiving, do we have an idea of the percentage of those that have this deletion within them, within the United States?

CRYSTAL GIGANTE: It's a very small number. I would have to see how many have been identified. But it's a handful. Fewer than 10 cases total have been identified that I'm aware of. One of those cases was identified at CDC, so that's why I don't have the exact numbers. But yes, it is a very small number of the total cases.

SEAN COURTNEY: OK, great. Thank you so much for that, Crystal. And thank you again for joining our call today and sharing this information. And so we'd like to ask you if you can just hang out on the rest of the call, if you're able to, and if any additional questions come up in the Q&A function that you could kind of take care of those within that feature.

But we're going to move on to our next presenter, and we have Carly Adams. And she is from CDC's Division of Foodborne, Waterborne, and Environmental Diseases and she'll be discussing the wastewater surveillance for monkeypox. And Carly, ready for you now.

CARLY ADAMS: OK. Hi, everybody. Can you hear me?

SEAN COURTNEY: Yes, you're good.

CARLY ADAMS: OK, great. Thanks. So hi, thank you for having me today. My name is Carly Adams. I'm an Epidemic Intelligence Service, or EIS, officer at the CDC, and I joined the National Wastewater Surveillance System team at the CDC earlier last month. And today I'll be presenting on the National Wastewater Surveillance System, or NWSS, opportunities, and challenges for wastewater surveillance for monkeypox. And I, like Crystal, I'm also a little bit sick. So I'm sorry if I'm a little congested. Next slide, please.

The National Wastewater Surveillance System was first launched by the CDC in September 2020 to detect and quantify the presence of SARS-CoV-2 in the United States wastewater. Since then, news has grown rapidly, providing CDC funds to 46 states, five major cities, and two territories for wastewater surveillance activities.

To scale up quickly, the CDC has also partnered with a commercial contractor that services 367 sites nationwide, prioritizing vulnerable communities. All these data are reported to the CDC, with data from over 83,000 unique wastewater samples reported, representing over 130 million people, or about 50% of Americans on a sewer system.

And this map here is showing zip codes with wastewater sampling, from April 2020 to August of this year. And you can see just how quickly news has expanded, in part due to this commercial contract. Next slide, please.

Wastewater surveillance can be a really powerful tool that can be used to complement more traditional case-based surveillance methods. First, it can capture asymptomatic infections and more mild infections in individuals that may be less likely to seek medical care, and therefore less likely to be diagnosed and reported as a case.

Wastewater surveillance data is independent of health care seeking behavior and testing access. Wastewater serves as an efficient pooled sample of community or sub-community infections, with sub community including things like correctional facilities, long term care facilities, universities, and schools. The data are available quickly, which I'll go over more in a few slides, and there's a flexible platform that can be leveraged for multiple pathogen targets. So for news, the data structure is set up so that multiple different pathogens can be reported using the same underlying data structure. Next slide, please.

There are several examples of successful uses of wastewater data for the COVID response. State and local jurisdictions have used wastewater data to inform response decisions, such as independent confirmation of true increase or decrease in cases. Public messaging, so informing the public of wastewater trends so that individuals can assess their risk of contracting COVID and make informed decisions based on that risk.

Distribution and siting a test capacity, so determining when and where to increase COVID testing efforts. Surveillance data in communities where clinical testing is limited or not available. Near-term forecasting of cases or hospital use. Monitoring the impact of home testing, because with the proliferation of at-home COVID tests, only a small fraction of positive results are now being reported to public health agencies. And detecting the emergence of variants of concern. Next slide, please.

As I mentioned previously, one benefit of wastewater data is its timeliness. From this schematic here, you can see just how quickly wastewater data can be communicated to the public. So first, someone uses the toilet on a sewer system. Then a sample of untreated wastewater, or sewage, is collected, usually as it flows into a wastewater treatment plant.

About three days after sampling, the sample is processed. Data are then generated, showing viral concentrations in the wastewater. Data are submitted to the CDC, and then data are communicated to the public, which is only about seven days after sampling. And rapid turnaround time is key for public health action.

We use a system called DCIPHER, or Data Collation and Integration for Public Health Event Response, which is where all data are submitted. And DCIPHER provides automated reports to our partners about any data errors to ensure that the data are high quality. This all gives us fast quality data that can give lead times of up to four to five days in clinical cases. Next slide, please.

And this here is showing a screenshot of the news DCIPHER data dashboard. And each dot here represents a site that has reported data in the past 15 days. This is where news partners can go to view the data. This dashboard is not public-facing, but there's also a public-facing dashboard called the COVID data tracker, which includes all these same metrics, except for the variant-specific metrics.

Partners can look at several different metrics on the dashboard, including percentiles, which are site specific and show the relative levels of virus present in a community. Percent change, which is shown on the map here. And this is the magnitude and direction of virus levels in a community.

Detection proportion, which shows how frequently the virus is detected in a community. And for now, this metric isn't super helpful because almost all the samples are positive. But hopefully this metric will have some more utility in the future. And most recently, there are variant-specific metrics, which show if a known variant is present and at what proportion. Next slide, please.

And this is showing the variance metrics that I just mentioned. On the left, the dominant variant of concern is shown. And on the right, you can see trends in the dominant variant of concern for one site, which is shown by the colored bar on the bottom. And then this trend line is showing the SAR-CoV-2 levels in the wastewater. And the stars represent samples that were sequenced, which was about 50% of the samples shown here. Next slide, please.

Now shifting from COVID to monkeypox. Monkeypox virus DNA may be shown in stool and urine, as well as other fluids that could be captured in untreated wastewater. The testing platform is flexible and the news team is now working to validate a protocol for testing of influent wastewater from monkeypox DNA. This will give us quantitative levels of DNA over time to monitor for trends. But these tests won't tell us if the virus is viable or infectious. And as I mentioned earlier, the data pipeline is adaptable and news has developed a method for integration of monkeypox wastewater data into DCIPHER. Next slide, please.

Some academic groups and health departments are doing their own testing for monkeypox in wastewater, and there have been several recent reports of detection of monkeypox virus DNA in wastewater in several states. The CDC is working with these academic groups and health departments to learn more about these reports.

We've confirmed that evidence of monkeypox virus DNA is present in wastewater samples. On the right here, you can see monkeypox virus DNA levels over a period of about four weeks from wastewater plants in California.

Clients represent the daily values and open circles indicate non-detects. So they detected monkeypox virus DNA from nearly all the nine wastewater plant samples. The next slide, please.

For future directions from the monkeypox response, we're adapting our testing and data platform to monitor for monkeypox, in addition to SARS-CoV-2. And because the platform is really flexible and already set up to receive data from pathogens other than SARS-CoV-2, we're just testing the platform now and we'll continue to test it as we receive more data.

This wastewater surveillance can help us monitor for disease at the community level, with a single sample representing communities of hundreds and millions of individuals. And this will require close partnership with case surveillance and health departments because these data should be used to complement, and not replace, case-based surveillance methods. Next slide, please.

Thankfully, the last one. I'll end with some challenges and research gaps. So some of the questions we still need to answer. How many people in a community would need to be infected to be able to detect virus in wastewater? So in other words, what is the limit of detection?

How long do signals last, and how do they correlate to clinical case counts? So if someone is shedding for long periods of time, such that wastewater concentrations are more indicative of prevalence as opposed to incidents, then wastewater data may not correlate well to clinical case counts.

What does it mean for a community if the virus is detected in their wastewater? So what public health action, if any, should be taken when there are monkeypox detections? What lab method would be best for detecting virus in wastewater, and is monkeypox virus viable and/or infectious in untreated wastewater? And this is important for utility worker safety. And then also from a zoonotic perspective. So whether wild animals are at risk of also becoming infected. Next slide, please. And with that, I'll take any questions. I'm so sorry. Thanks.

SEAN COURTNEY: Oh, it's not a problem. Thank you so much, Carly. And I really appreciate you joining our call today also while feeling not so great. So we really appreciate your participation today. I don't see any questions right now in the Q&A feature, so I'm not going to make you answer any more.

But if any pop up, if you can type out the response within the Q&A function, and that'd be great. But again, really appreciate your participation today, and also hope you feel better. So thank you.

CARLY ADAMS: Thank you, yeah. Thank you for bearing with me through that. I'm so sorry.

SEAN COURTNEY: You're great, thank you so much. I appreciate it. All right, and with that, we're going to move to our next presenter and that is going to be Tim Stenzel with FDA. And Tim, I'm going to stop sharing my screen so that you can share slides from there.

TIM STENZEL: Sounds great. OK, Sean. Can you see my screen?

SEAN COURTNEY: Yes, I can.

TIM STENZEL: Oh, fantastic. I haven't had great internet connection today, so it'll be much to do with voice and showing this. I'm going to stay off camera. So many of the callers today may have called in to the FDA town hall call last week on monkeypox, their first call with well over 500 developers were called in.

But just in case there's significant numbers that didn't attend that call, I wanted to briefly go through our presentation that we did on monkeypox and the guidance for tests that we issued about September 7. So this is the introduction slide, and I'll share these slides with the CDC so they can post the slide deck, so that participants today can have these links and email addresses.

So the first email address is for any developers that have any questions about monkeypox. They can email the FDA at this email box. The second one has to do with signing up for webinars, or town halls in this case. And there is a monkeypox one and you can be kept up to date with the schedule of town hall events for monkeypox.

And then finally, if you want to submit a question prior to an upcoming monkeypox town hall call, you can email at CDRH Webinars, and we'll get your question ahead of time and be able to prepare an answer for mentioning on the call.

So on September 7, in response to the declaration from the Secretary of HHS-- we're now designated under EUA authority. So they weren't previously, even though there had been a public health emergency declared by the Secretary under the Public Health Services Act.

The test authorities had been given to the FDA to use EUA authorities, which basically allows the FDA to lower the bar considerably for what is needed for test reauthorization. So there is a lot of information about all of this. The declaration for use of IVDs, the guidance in the EUA process.

And I'll let you just explore this when you get the slide deck. We have prepared a template for molecular developers that's available on the FDA website, and anybody has access to that now. It was a frequently asked question, and then I mentioned the story about the virtual town halls and how they handled that. So the guidance that was issued on September 7. That policy describes our review policies for what we will accept for review. It describes our enforcement policy for certain tasks that are developed by and performed by a single site laboratory certified under CLIA that meets requirements for high complexity testing.

So at the very beginning of monkeypox, the FDA made clear that we were going to provide enforcement discretion for monkeypox LDT tests. This has basically continued into the present situation when it applies to test. That is a single site, high complexity lab that uses a molecular PCR-based testing for monkeypox, and it's a lesion swab.

So the only thing we ask of those labs is that they notify the FDA per the email address that I gave earlier. And the information that's in the guidance that is needed, which is basically lab name, lab director, test name, things like that.

So as far as tests that we do-- and by the way, those LDTs that have PCR and lesion swabs and notify us, they don't need to send us any data. They don't need to send us their validation. They just need to notify us that they validated their test and their testing.

And there is no review. So we didn't want to limit the LDTs, in this case, to having to submit data. But for those that do-- that do require an EUA submission-- particularly the kit developers-- we wanted to make sure that they were made by manufacturers that could produce the kits at volume, and that the throughput of the assays in total.

All of the sites that might be testing something was high. For home collection-- so if an LDT wants to add a home collection then we want to see a submission. And then, of course, rapid test, point of care test. And we are looking primarily for experienced developers in the manufactured kit space.

And we would like them to notify us within 30 days of the guidance of their interest to submit an EUA, and their plans. And we would review those plans and let them know whether they are invited for submission. For labs, I went-- I went through this pretty much already. You have what you have to do for CLIA. But again, we don't need to see the data. There may be rare cases when we reach out if we hear something, but that's not our intent. And I went through the manufacturer's plans as well, so let's get through that.

I mentioned the templates. We have developed a template for central lab molecular diagnostics for monkeypox. There's a short version and a long version. We are planning an antigen template, and we are planning a home collection template. But if you have interest in any of those modalities, you can reach out to the FDA at the monkeypox email address.

One thing about serology tests. So there isn't a demonstrated need for serology tests at this moment, but we did want to make sure that primarily academic medical centers have the opportunity to perform research and potentially perform some clinical testing. We want to make that clear, again, labs that fit this criteria simply notify the FDA of your validation and include certain information that's present in the policy guidance.

We did hold our first webinar, as I mentioned, last week, and there's additional links and valuable information in the slide deck that will be shared. And with that, I'm happy to take any questions about monkeypox test development.

SEAN COURTNEY: All right, thanks for that update, Tim. Really appreciate it. The first question we have is, when HHS-- when the HHS Secretary declares the COVID public emergency over, what becomes of

the COVID lab tests that were authorized by FDA under EUA but have not been submitted for FDA approval or clearance?

TIM STENZEL: So for COVID, the LDT tests needed to be submitted to the FDA for review. Now not all of them-- they're allowed to be on the market if they were a notified test while the FDA reviewed them. So-- and as far as what will happen with those LDT tests when the test declaration is removed-- and I'll repeat that the public health emergency for COVID is separate from the EUA test authority.

So there is a desire, often, on the part of the US government to allow continued access to EUA authorized tests. We've done that for-- we've done that for Zika, we've done that for Ebola. There are EUA authorized tests that are still able to be used under US authorities for those emergencies.

Those FDA statute declarations for EUA tests are still in effect. So I don't know when the test authority will be removed, but we have drafted and published a draft guidance for the transition plan that will detail all of these things. And we are now working on the finalization of that guidance, so it'll have to wait until that guidance is finalized.

SEAN COURTNEY: All right, thank you. Next question I see is, is there a need for making positive diagnostic calls based on two different targets in the genome, rather than just one? Would that be a requirement for any diagnostic developer, in addition to the positive control? So that's kind of more in line with a concern around the deletions that have been discovered.

TIM STENZEL: Yeah, the FDA is tracking mutations in monkeypox. And for those tests where we know the design features, to date, we know that for the Quest EUA that's been authorized, we know that for the CDC assay. We are tracking the impact of monkeypox mutations on those tests.

And so far, there is no indication that the CDC NVO test is impacted by any mutations. But because we as well have observed these deletions in the monkeypox, that has knocked out some of the monkeypox specific LDTs. We are encouraging developers to use multiple targets. We have been doing that encouragement for COVID for a long time.

We think it makes sense. But there's not a recommendation for-- that two targets be used in assay development. It's just an encouragement at this point.

SEAN COURTNEY: All right, thank you for that. I really appreciate that clarification. And I don't see any other questions right now, so again, I appreciate your participation on today's calls and all the previous ones. And again, I just want to thank all of our speakers today for their participation, and I just want to remind everybody that our next call is going to be on Monday, October the 17th at 3 PM.

And so again, it's really-- we want to thank everybody for joining us today, and we continue to be grateful for all of your work. And we'll talk to you again on Monday, October 17. Thanks, everybody.