Transcript

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Welcome
Sean Courtney
CDC Division of Laboratory Systems

Marburg Virus Disease Update
Joel Montgomery
CDC Division of High Consequence Pathogens and Pathology

SARS-CoV-2 Variants Update
Natalie Thornburg
CDC Coronavirus and Other Respiratory Viruses Division

FDA Update
Timothy Stenzel
U.S. Food and Drug Administration

Use of Laboratory Preparedness Exercise (LPX) to Assess Rule-Out/Referral Capability of Clinical Laboratories
Chris N. Mangal
Association of Public Health Laboratories

Sean Courtney: All right. Good afternoon, everybody. Go ahead and get started with today's call. So good afternoon. My name is Sean Courtney. And I'm a Health Scientist in the Division of Laboratory Systems here at CDC. On the screen is the agenda for today's call. But before we get started, I want to just cover a few announcements and some general housekeeping items.

As you've heard on previous calls, DLS is a CDC division that works 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.

So announcement for today is the CLIAC spring virtual meeting that will be held on April 12 and 13 from 11:00 to 6:00 PM each day. The meeting agenda will include updates from CDC, CMS, and FDA. Presentations and discussion will focus on reports for the CLIA regulations assessment workgroup, the CLIA Certificate of Waiver and Provider-performed Microscopy Procedures workgroup, and the laboratory's role in advancing health equity. CDC encourages attendance at the CLIAC meeting and participating in public comment. More information about the meeting can be found on CDC's CLIAC website.

And as always, we'll be sharing slides from today's call along with audio and transcript. And we'll post them online, hopefully as early as next week. You can find them on CDC's Laboratory Outreach Communication Systems (LOCS) page at the link shown here on this page.

And so we want to hear from you. Our training and workforce development branch is interested in hearing more about the 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 any questions, we'd like to ask you to please use the Q&A function within Zoom so that we can address it during the call. And we ask that you please do not use the chat function. Also, we'd like you to please include your email so that we can follow up if we're not able to address your question during the call.

And if you're from the media and have any questions about the presentation or would like to follow up or use content from today's presentation, we ask that you please reach out to CDC media relations at media@cdc.gov. And if you're a patient, please direct any questions to your health care provider.
And lastly, I'd like to remind everyone 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 positions on the topics covered.

And so with that, I'd like to move to our first speaker today, which I think was supposed to be Joel, but I don't think he was able to join us yet, so I'll come back to him and move forward with Natalie Thornburg, who is going to give us an update on SARS-CoV-2 variants. And so Natalie, I will stop sharing my screen and hand it over to you.

Natalie Thornburg: OK. Thanks, Sean.

Sean Courtney: All right. You should be good to go.

Natalie Thornburg: All right. You should be seeing my screen. You should be seeing the COVID data tracker. So cases, deaths, and hospitalizations for COVID-19 have been decreasing steadily over the past two months. As testing behaviors have changed, our case counts, our absolute case counts, has become a little bit less accurate of community transmission of the virus, and therefore, we've been looking at both total case counts as well as percent positivity to indicate circulation of SARS-CoV-2.

And so this is the total case counts, y-axis time back to January 2020 to the present. Blue are the case counts. And then orange is the test positivity. And that is the right y-axis. And so you can see we saw a peak of test positivity right after the holidays, January 4. And that has been decreasing steadily and is sitting at somewhere around 7 and 1/2% of percent positivity.

This is data from our genomics data tracker. A month or two ago, we changed the way that this looks. We have separated out the weighted estimates from the Nowcast models data. So the weighted estimates is this area on the left side of the genomics data tracker. And we calculate the proportion of circulating lineages from actual sequences deposited into databases in sequences received and performed by us to establish the weighted estimates.

So those are actual sequences and actual sequencing data. Because of the turnaround time of identifying positive specimens, transporting those specimens to sequencing labs, getting a sequencing assays completed, which is a several-day process, a genome assembly transfer of data analysis, there's always going to be a delay in that genomics data. And therefore, we use the weighted estimates to calculate growth rates. And those are used for Nowcast data.

And those are shown in the three bars on the right. The data in Nowcast is model data, not actual sequencing data. And those-- so Nowcast is used for the three most recent weeks of genomic proportions. So XBB.1.5, which is a BA.2 lineage virus, has been the predominant circulating viruses nationally for quite a while now.

It is sitting at about 90% of circulating viruses nationally. It has been diversifying over the past month, month and a half because it's just the predominant virus. And we recently broke out a sub lineage from XBB.1.5, and that one is shown right here, XBB.1.5.1.

That virus has one additional change in its spike protein in comparison to its parent lineage. And that change is-- sorry. Let me take a quick look. Remind myself-- is at position 573 in the spike protein. There has been some viruses circulating more dominantly internationally, XBB.1.9. That is not currently broken out on the data tracker. It is aggregated. It is in the data tracker, but is aggregated with its parent lineage, XBB. That virus that is predominant in some other parts of the world, it's XBB.1.9. So that is on the data tracker aggregated with XBB.

That virus has the same spike sequence as XBB.1.5. So it has the same spike sequence but evolved independently, meaning it is a convergent evolution. So it is in that XBB. And so nationally it, as well as other XBB lineage viruses, represent about 2, 2 and 1/2% of circulating viruses nationally.

Regionally, XBB.1.5 is still the predominant circulating virus in all regions. And that's this dark blue color. Some regions are showing higher percentages of some other lineages, though, for the first time in several weeks. Like region 7, for example, is showing a bigger prevalence of XBB viruses than, say, region 1 and region 2, although still a minority of circulating viruses. And that's really all I have to cover today.

Sean Courtney: All right. Thank you for that update, Natalie. Really appreciate that as always. I do not see any questions currently in the Q&A feature. But as usual, if you could just hang around on the call and answer any questions that may pop up, we would really appreciate that. So thank you. Thank you for today's update.

All right. So I just want to provide an update that unfortunately we have a scheduling conflict for today, and we will not be able to provide an update on the Marburg virus disease outbreak. So hopefully, we'll be able to have them join us on our call in April to provide that update. So with that, let me begin sharing my screen again. And we'll move on to an update from Tim Stenzel with FDA. Tim?

Tim Stenzel: Hello, Sean. So you and Jasmine asked if I could get an update on what's going to happen with the end of the COVID public health emergency (PHE) that's coming up, scheduled to be on May 11 of this year.

So there are authorities that go along with the public health emergency that the secretary makes. And that happens to be separate authorities and not connected to the emergency authorities associated with countermeasures such as tests, like COVID tests, which is under Section 564 of the Food, Drug, and Cosmetic Act. So it's a separate declaration, and it is not connected.

In fact, you can have 564 test declarations without a PHE declaration. And likewise, the 564 authorities can continue after the discontinuation of the public health emergency. In fact, this is happening right now for Ebola and Zika and for other previous 564 declarations.

And the tests that were authorized under EUA are still able to be offered for those that were authorized. And they're listed on the FDA website. So in talking about what would happen, what would bring the 564 to an end-- and there is planning for it. And there is a draft guidance out there that describes the transition period between the end of a 564 declaration and what would happen before tests would-- might have to be taken off the market, and in particular, commercial kits that are currently on the market.

So the FDA would like to see that many more test kits are converted to full authorization. And then this would allow tests to stay on the market after the end of the 564. The reason why 564 authorities are likely needed beyond the end of the PHE is that we haven't had enough submissions and enough authorizations, full authorizations, clearances, basically, of tests so that we can supply-- so that the nation has a supply of authorized tests that can continue to use for COVID.

So we are encouraging submissions. And we are reviewing the ones we have. And we have been making such authorizations. The most recent was De Novo grant for a point-of-care antigen test. And that was the first antigen test that was fully converted. And so we just need to see more so that we know there's assurance of long-term availability of authorized test kits for COVID.

Of course, the Mpox public health emergency ended on January 31 of this year. And the 564 declaration for Mpox remains. And that's very important because very few of the EUA authorizations were even authorized on prospectively collected Mpox samples. And to be able to do a prospective study now to collect some of those needed prospective samples with Mpox numbers being so low, which is good, would be obviously nigh on impossible.

So it's quite likely that the 564 Mpox declaration will remain in effect for probably a very long time. Anyways, that's the update, Sean. And happy to take any questions.

Sean Courtney: All right. Thanks, Tim. I really appreciate you explaining these different PHEs and any actions that can and cannot happen after them. So there are a couple of questions in the chat. And I'll

kind of go through maybe one or two of them. First one is does the 564 have a scheduled or predicted end date yet?

Tim Stenzel: No.

Sean Courtney: All right. Thank you. Sorry. I'm reading through these real quick.

Tim Stenzel: That's fine.

Sean Courtney: I think you just kind of answered that one. All right. Well, those are the only ones we have right now, actually. So appreciate you joining today's call. If you can hang out if you're available and answer any additional questions that may pop up in the Q&A, we really appreciate that.

Tim Stenzel: Absolutely. Thank you.

Sean Courtney: Thank you. Thank you again for this. All right. So moving to our next speaker, I'd like to introduce Chris Mangal from APHL, who is going to provide an update today on Laboratory Preparedness Exercises. Chris?

Chris Mangal: Sure. Thank you, Sean. I appreciate it. Thanks to the CDC DLS team for inviting me to present on this call. Happy to discuss how we utilize the Laboratory Preparedness Exercise, or LPX, to assess, rule out, and referral capability of sentinel clinical laboratories. Next slide, please.

So today, I'll provide a brief history of the Lab Preparedness Exercise, how it's evolved, and how we currently utilize this exercise. I'll also touch on some challenges we've observed with the exercise and certainly open it up for some Q&A on how this exercise is working within the clinical laboratory community. Next slide, please.

So a little bit more about the Laboratory Preparedness Exercise. It originally started out as a Laboratory Preparedness Survey. And one of the things that we ran into was a terminology or use of the word "survey" and whether that was seen as a proficiency versus an exercise. So when this all started, it was around 2003, and it took us a number of years to sort of just get it right and get the exercise to mirror the SOPs and mirror practices in other training programs.

In about 2008, the name was changed from the Laboratory Preparedness Survey to a Laboratory Preparedness Exercise. It's issued by the College of American Pathologists, or CAP. And this biannual exercise was a much-needed tool that has been maintained since 2003 to really look at how we assess sentinel laboratory preparedness.

When it was originally developed, there were a number of concerns, including the use of photomicrographs, organisms that weren't necessarily reflective of biothreat agents, and also it did not

align fully with the Laboratory Response Network (LRN) sentinel level clinical lab protocols that is maintained by the American Society for Microbiology (ASM).

Another gap was that it did not require a notification of the LRN reference laboratories or public health labs. And so over time, we worked with CAP to ensure that these issues or these concerns were addressed. Next slide, please.

Thank you. The CAP exercise is really a strong partnership with APHL, CAP, and CDC. And each of these partners have a unique role in putting together this exercise. APHL really focuses on the public health laboratories in ensuring that we are sharing guidance with the public health labs and encouraging the public health laboratories to engage with the clinical laboratories and also to use the exercise as a test of their system.

CAP is focused around administering the exercise. What that means-- it's development of the exercise. So the kit instructions, the materials used in the exercise, they're also very much focused in communicating the exercise to the clinical lab community, so they create public announcement, and they lead in all promotion and communication activities.

CAP also analyzes and publishes summary results. And one of the things that we do is that we do work closely behind the scenes with CAP to ensure that we are sharing those results from select clinical laboratories that approve us to receive those results with state public health laboratory directors.
CDC is at the table providing technical assistance for issues related to the content of the exercise, so for example, the organisms that would be utilized in the exercise. They also provide subject matter expertise, and they ensure the accuracy of the organisms being utilized. When appropriate, they provide antimicrobial susceptibility testing. And they are also at the table helping to ensure the safety of the organisms. Next slide, please.

One thing I wanted to note was that the three partnerships, if you will, has been around-- it was initiated back in 2005. And it has been formalized since 2006 and continues today to ensure that we can issue the biannual LPX. Big picture-- the purpose of the LPX is to provide labs with an educational exercise. And that educational exercise is really focused around being able to refer or rule out agents that could be used as a biological threat.

One of the things that we have focused in or honed in on in recent years-- it's a notification component of this exercise. So if, for instance, you are unable to rule out a BT agent, there's a specified time frame where clinical laboratories would then notify the public health agency, which is typically their LRN reference level laboratory.

We see this exercise as having the ability to test most aspects of laboratory BT response. It's the rule-out and referral component using the ASM sentinel protocols. It's also looking at the notification component that I mentioned. There is the potential for laboratories to use this to test the ability to package and ship specimens. Again, it's not a proficiency testing, so it's not a proficiency test. So clinical laboratories can

certainly package and ship those particular isolates to their public health laboratory or LRN reference level laboratory.

We're also looking at biosafety. So anyone participating in this exercise must have a Class II biological safety cabinet in order to be able to accept those isolates and perform the procedures. And from the other side of things, looking at the LRN reference level laboratories, they can utilize the exercise to identify gaps in preparedness. They can look at what specific training programs they should be developing or implementing to support sentinel clinical laboratories.

And as mentioned earlier, they can test the ability of sentinel labs to package and ship, but they can also utilize the exercise to assess the internal search capacity of the public health or LRN reference level laboratory. Next slide, please.

A little bit more about the LPX. It's biannual. And it's typically issued April and September. The participation rate varies. On average, we see about 1,200 laboratories participated in each exercise. And for laboratories that subscribe to the LPX, CAP sends live organisms that exhibit characteristics of bioterrorism (BT) agent, or they demonstrate public health significance.

Labs are expected to respond following the ASM sentinel level clinical protocols. And that response, again, encompasses the notification component. And all agents that are provided as part of this exercises, they are excluded from CDC select agent list.

One of the things I'd like to note here is that we are in the process of working with ASM to review and update some of these protocols. We recognize that some of these SOPs are outdated. And so we are taking a very close look at them and will work with ASM to provide more current SOPs. Next slide, please.

So what are some of the challenges that we've seen? I've discussed the benefits in terms of how we utilize the exercise to test the system. Some of the challenges that we've observed while conducting these two exercises have been the shift from the use of biochemicals to more automated systems and use of the automated system, such as MALDI-TOF, and seeing misidentification of some of the organisms that are included in that exercise.

We're also seeing some biosafety concerns in that by using the MALDI system, there is a potential there for laboratory exposures. And so we have updated the guidance on the exercise where its specific language is provided in terms of how a laboratory should extract the organisms, what are the specific filters that should be used before placing the organism on the MALDI-TOF.

And one of the other challenges that we've seen is communications. So you've got the use of these automated systems. You've got the biosafety concern. And then we have some communications challenges where the laboratory, the public health agency or the public health laboratory is not contacted within a designated time frame. Next slide, please.

This is an example of one of the recent communications challenge, where you can see-- so this figure shows the interval between the guidelines initiated and then the report to the LRN reference lab for *Francisella tularensis*. And something like this, they should be reported between 48 to 72 hours. And here we see hundreds of laboratories going past that three-day window to notify public health labs.

And so something like this, what we would do is step back, take a look at it with the state public health laboratory, and say this is an area where you've got to work more closely with clinical laboratories on and what training and what additional guidance can APHL, CAP, and CDC help to provide you and ensure that you're sharing that information with your clinical labs as well.

We're seeing this communication issue not just related to the LPX, but we're seeing some of those communication issues with other real-life pathogens. As well and that's something that we'll be discussing with our Public Health Preparedness and Response Committee and other partners to really look at how we can provide better guidance to step up the notification aspect and not see this gap in notification. Next slide, please.

So a couple of resources for folks-- and I'm happy to also share additional information on how we use the LPX. My contact information is at the end. You can reach out to me. But some of the resources that I'd like you all to be aware of-- it's obviously the CAP site that provides more information on how you can purchase the LPX. The ASM site that houses the LRN sentinel clinical lab protocols, and then the BMBL 6th edition.

APHL also has a number of references, which include the definition of sentinel clinical labs. And the simplest way to understand that definition-- it's really we are focused on a subset of clinical labs that perform high complexity testing. We provide a number of tools, including the biothreat agent identification bench cards. Those templates are available on our site. They can be downloaded and utilized in laboratories. Same for the biothreat agents poster.

And then lastly, we work really closely with a number of our state and local public health laboratories to maintain what's called the Clinical Laboratory Preparedness and Response Guide or sort of the old designation, the BT Blue Book. And that has an A to Z-- a very comprehensive list of all resources for clinical laboratories in this biothreat space.

We are currently in the process of updating the Clinical Lab Preparedness and Response Guide. It was updated in 2018. But we're reviewing and updating it once again. And once that's published, we'll be sure to share it with Sean and DLS to get that out to you as well. Sean, the next slide has my contact information. So I'll go ahead and stop there. And happy to take any questions related to the LPX.

Sean Courtney: All right. Thank you so much, Chris. Really appreciate you joining our call today. Trying to get through the questions real quick. Just one second. Sorry.

So one of the first questions is, is a delay in communication of results due to delay in identifying the BT or other reasons resulting in delayed communication?

Chris Mangal: I'm not entirely sure of the answer to that. It could be maybe perhaps a delay in observing growth. What we're hearing is some of it may be the loss of biochemicals in the laboratory. So some of those, I want to say, preliminary test that you may do within the laboratory, those tests are not being performed. So there's a lag that's happening there.

But I think we want to dive a little bit deeper into the most recent LPX to see why did laboratories take so long to notify public health of Ft [*Francisella tularensis*].

Sean Courtney: All right. Thank you. The next question's not necessarily a question, maybe more of a comment. Not sure if you want to respond to it, but I'll just read it. It says my lab doesn't accept CAP LPX results unless the clinical lab has all three results. So this may cause some of the delays. And having the labs report each individual result as they get them would not be manageable for the staff receiving the calls.

Chris Mangal: Thanks, Sean. And Danielle, I don't disagree with you on that. But I think part of this exercise is to be as realistic as possible. And so part of what we have to do is step back and think of how can public health laboratories be more supportive of the clinical laboratories in being able to accept those calls. And I think we've got significant staffing issues, where public health just does not always have the staff to be able to accept those calls, as Danielle has mentioned.

So I appreciate that comment. And this is something we will definitely take back and have some more discussions with other partners. But we have to really look at this as it's the exercise-- we've worked very hard to get this exercise to be as realistic as possible. And part of that realistic aspect is communications. It's being able to accept those calls.

Sean Courtney: Excellent. Thank you. Next question is, are the specimens limited to bioterrorism agents?

Chris Mangal: They are mostly sort of-- and I want to call them mimic organisms or attenuated strains of bioterrorism agents. We have, over time, broadened it to where we may look at agents of public health significance. So it has evolved. And it will continue to evolve beyond the BT agents.

Sean Courtney: All right. Thank you. Next question is are COVID testing labs, do they fall under sentinel lab category?

Chris Mangal: It really depends. It depends on whether or not they are-- what's their status under CMS CLIA or the Department of Defense CLIP. So if they have this high complexity, their ability to perform high complexity tests, then they would be considered a sentinel lab. And some of this has taken a look at your

lab facility. Do you have a Class II biological safety cabinet, in that can you actually safely accept these isolates and perform testing of it?

So I don't believe that all COVID testing labs would fall under this designation because we've got a lot of waivers in place for COVID labs. So it really depends on the ability to perform the high complexity test.

Sean Courtney: All right. Thank you. So the next question is, since MALDI-TOF is becoming the standard in most microbiology labs, is there any push to add the BT organisms package for sentinel labs in providing guidance for usage there?

Chris Mangal: I think we started small by doing some studies to first look at how you can safely work with these organisms on MALDI. And we've published that in the Journal of Clinical Micro. I think the next phase is now taking a look and seeing many, many clinical labs, absolutely correct. They are using MALDI-TOF.

How do we adjust these sentinel protocols to account for automated systems such as MALDI? So we're in that phase right now of having a discussion of how can we adjust our SOPs to account for MALDI and then look subsequently at software and so forth. But we have not yet reached any sort of agreement that this is the path to go. So in discussions, but no solution at this time.

Sean Courtney: All right. Thank you. Another comment is that there are severe shortages of microbiologists in the laboratories. And the question is, does APHL have any online trainings? And before you get to that, I'm also going to add that CDC also has CDC TRAIN that can provide training online. And I think we're going to drop it in the chat as well. And I'll put that question to you regarding APHL's online training opportunities.

Chris Mangal: Thanks, Sean. And there are a number of training courses, but most of them are offered through CDC TRAIN, and I would highly recommend those courses. Your public health laboratories also will have in-person training, but I recognize it certainly doesn't meet the need when you've got short staff. They can't leave and attend these courses.

So we'll take a look and see what public health labs-- and Sean I can share that with you. Because some public health labs do offer virtual training courses as well. I will emphasize that our preference for these are the wet workshops where people are coming in person to do these types of training courses.

I can take a look and see if these are still up, but I believe that places like Iowa, they've also done virtual exercises, where they're able to simulate some of these SOPs. And so we can take a look at if Iowa has still maintained those virtual exercises.

Sean Courtney: All right. Great. Thank you so much for that, Chris. And thank you for joining today's call. Really appreciate you being on here talking about this program and answering all the questions. So obviously, there's a lot of excitement around it. So thank you for that.

I was going to go back to Tim, but I see that he was able to answer some of the questions that came up after his talk. So I appreciate that, Tim. And with that--

Tim Stenzel: Could I answer one question a little bit more?

Sean Courtney: Absolutely. Go ahead.

Tim Stenzel: It's hard to type in there. So this is the conversion from an EUA-authorized test to a full authorized test. When that happens, we remove the 564 authorization for that test, and we ask the manufacturer to notify their customer base. So if you're a customer of an EUA test, and it gets fully authorized, the manufacturer of that test should notify you. And there will be a conversion period where you can continue to use the EUA kits before, hopefully, until they use them all or the expiration date is hit.

Then you can convert to the fully authorized test so that it's an efficient process. You don't have to spend extra money and waste the kits that you might have. So the FDA takes a look at this. We care about that. We care about making life as easy as possible for labs that are using EUA test kits now and want to have access to EUA tests.

Sean Courtney: All right. Thank you. Thank you for that explanation. Actually, another question kind of popped in right when you were finishing. It says, if you continue to use an EUA kit, do you still need to add the disclaimer to lab test results?

Tim Stenzel: I am not-- that this is an EUA test and it's not been FDA cleared or approved. I think that's probably what they're talking about. So as long as it's an EUA-authorized test, continue to use the disclaimers that are recommended to go along with that. But when it's fully authorized, then it's like any other normal test kit you buy that's FDA-cleared or approved. And you follow what you normally do with a fully authorized kit.

Sean Courtney: Thank you. I appreciate the clarification there. And thank you for jumping back on to answer that question. Really appreciate that. All right. So I guess that ends today's call. So I just want to again thank all of our speakers. And as a reminder, we typically hold these calls on the third Monday of each month. And they're scheduled from one hour, from 3:00 to 4:00 PM.

And our next call will be held on Monday, April the 17th. Please let us know if you have any suggestions for future topics on calls. And we look forward to continuing to discuss anything that kind of pops up, any hot topics that we have, as well as answering your laboratory and testing community needs.

As I mentioned at the start of this call, we'll post the audio and transcript and slides from today's call on the website, hopefully by next week. And so you can find us on social media through Facebook, Twitter, Instagram, and LinkedIn. And so please follow them to stay up to date with the latest news and recommendations.

And before we conclude today's call, I wanted to briefly mention that Lab Week will be on April 23rd to the 29th this year. Every year at DLS we highlight Lab Week to honor our laboratory professionals for their contributions to public health and patient care. And featured on the screen today is our graphic from last year's Lab Week campaign, where the theme was “Giving the Gift of Health.”

And so this year we'll have a new theme paired with really cool graphics that are going to be tailor-made for Lab Week. And we're really excited to share our upcoming Lab Week activities and how we're celebrating the work of lab professionals on our next LOCS call on Monday, April 17.

So again, I want to thank everybody for joining us today. And we continue to be grateful for all of your work. So thank you all and look forward to talking to you next month. Have a good one.