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Call Agenda
Welcome

Sean Courtney, CDC Division of Laboratory Systems

ISO 35001:2019 – Biorisk Management for Laboratories and Other Related Organizations Standard

Folasade Kembi, CDC Division of Laboratory Systems

Mpox Update

Christina Hutson, CDC Division of High-Consequence Pathogens and Pathology

Mpox Reporting Update

Shaw Gargis, CDC Division of Regulatory Science and Compliance

Early Detection and Surveillance of the SARS-CoV-2 Variant BA.2.86

Anastasia Lambrou, CDC Coronavirus and Other Respiratory Viruses Division

Call Transcript
Sean Courtney: All right. Good afternoon, everybody. We can go ahead and get started. Thank you for joining us today.

My name is Sean Courtney. I'm a Health Scientist in CDC's Division of Laboratory Systems, and on the screen is the agenda for today's call. But before we get started, I just want to cover a few announcements and some general housekeeping items.

So as you've heard on previous calls, DLS is the CDC division that works closely with clinical and public health laboratories across the country to support laboratory emergency preparedness and response activities, and we've 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.

As always, we'll be sharing the slides from today's call, along with audio and transcript, and we'll hope to have them posted online within the next two weeks. You can find them on the LOCS page, at the link shown here on this slide.

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 we invite you to send your feedback to labtrainingneeds@cdc.gov, shown here on the screen.

We'd also like to invite you to register for CDC's second annual OneLab Summit. It's a free three-day virtual event that connects laboratory professionals in real time to support a unified response to laboratory education and training needs. Attendance is open to anyone interested or involved in the laboratory profession.

This year's theme is “Thrive: People. Planning. Preparedness.” The event is designed for laboratory professionals to increase their knowledge of laboratory training, development tools and practices, gain insights from the clinical and public health laboratory community's success and resilience, network and collaborate with peers, laboratory professional partners, and CDC experts in laboratory education and training. Learn more about OneLab and its communities of practice, and you can earn P.A.C.E. credit as well. And you can register now using the QR code that is shown here on this slide, or that's going to be added to the link in the chat.

And so DLS has also launched the ECHO Biosafety Program-- that was back in January of 2023-- to develop and engage a community of practice to address biosafety challenges in clinical and public health laboratories. Based on the Extension for Community Health Outcomes (ECHO) Model from the University of New Mexico Health Sciences Center, this ECHO Biosafety Program fosters discussions on solutions for biosafety challenges, and its goal is to bridge gaps and build a community of practice in enhancing biosafety practices.

The sessions are designed for laboratory biosafety professionals, and the next session is actually scheduled for tomorrow, Tuesday, February 27, and will focus on *A Stepwise Process to Improve Biorisk Management Systems*. You can access the Zoom link, detailed information on upcoming sessions, and resources from past sessions through the ECHO Biosafety website link provided on the slide and in the chat. So please, contact dlsbiosafety@cdc.gov, if you have any additional questions.

And if you have a question today, during our presentations, we'd like you to please use the question-and-answer function in Zoom, so that we can address it during the call. We also like to ask that you please include your email, so that if we need to follow up, or we can't answer the question during the call, we have an option to follow up. If you're from the media, we ask you to please contact CDC Media Relations at media@cdc.gov, and if you're a patient, please, direct any questions to your health care provider.

And with that, I'd like to remind everybody that these 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 positions on the topics covered.

And so with that, I'd like to introduce our first speaker today. We have Folasade Kembi from CDC's Division of Laboratory Systems, where she'll provide us with an announcement about the ISO 35001:2019 - Biorisk Management for Laboratories and Other Related Organization Standards. Folasade?

Folasade Kembi: Thank you, Sean. Good afternoon, everybody. Next slide, please.

As part of the CDC's Division of Laboratory Systems commitment to biosafety and biosecurity, the Division of Laboratories System is offering free access to the International Organization for Standardization. ISO 35000 is entitled Biorisk Management for Laboratories and Other Related

Organizations. At this time, the offer is currently limited to interested laboratories and organizations within the United States.

I'll just tell you briefly about the standard, it was first published in 2019. It enables an organization to effectively identify, assess, control, and evaluate the laboratory biosafety and biosecurity risks inherent in their activities. It defines a process to identify, assess, control, and monitor the risks associated with hazardous biological materials. It is highly suggested for use in laboratories that test, store, transport, work with, or dispose of hazardous biological materials. Next slide, please.

So how do you apply for your own copy? The DLS requests that institutions or organizations that wish to gain access to ISO 35001 within the United States, designate a point of contact (POC) to facilitate the process. So the POC will initiate the access request by contacting dlsbiosafety@cdc.gov. The POC should either be a laboratory director, a biosafety officer, or its designee.

So when they contact dlsbiosafety@cdc.gov, they will notify us that they are interested. Then, they will provide the names of the people that are interested within their institution, their email addresses, and their role within the organization. Please, we prefer that they use work email addresses only. So this initiative will allow us to streamline the process and ensure that the Division of Laboratory System has an organized list of individuals that are interested and are granted access to the standard.

The Division of Laboratory System recognizes the importance of the ISO standard in enhancing biorisk management in laboratories and will encourage that your institution participate and have free access to this standard. Thank you, and we also encourage you to share the information widely within your network. Thank you. Over.

Sean Courtney: All right. Thank you for that update, Folasade. I do not see any questions in the Q&A currently. So I just want to, again, thank you for joining today's call and providing that information, so that any of our audience can reach out to get that standard. They have the information. So I do not see any questions, so I'm just going to say thank you, and we will move up to our next speaker.

All right. So please, welcome Dr. Christy Hutson from CDC's Division of High-Consequence Pathogens and Pathology, and she's going to provide us with an update on mpox. Christy?

Christy Hutson: Thanks, Sean. Thanks for inviting me today, and some of you have probably seen some of these slides. So I apologize for that, but I want to start with just an overview for those who have not seen this update on mpox. Next slide.

All right. So for those who are unaware of monkeypox virus and the two clades, this virus was actually first described in captive monkeys that had been caught out in the wild, within Africa, way back in 1958, and was first identified in humans in 1970. It is a zoonotic virus. However, we still don't know the reservoir. It's probably a small, African mammal, most likely a rodent.

It can be confused with smallpox, when smallpox was still circulating. You can see the pictures on the top right, that it caused a systemic lesion in some individuals that looked very similar to smallpox, and it's closely related to Variola virus. It is not related to Varicella. However, it can be confused with chickenpox, during current time, when chickenpox is still circulating within these areas.

There are two distinct clades of monkeypox virus. You can see the map on the right that shows the clade I and the clade II, and clade I has really been historically seen in Central Africa. It used to be called Congo Basin mpox because of the location it was found, and it has a mortality rate of up to 11%. This was a non-vaccinated individuals, more historic-- or sorry, more outbreaks that occurred at a more-- at a time period more-- Oh my gosh, I'm losing my words today, Sean.

So those were historic outbreaks. Some of the newer outbreaks-- there we go-- actually had a lower mortality rate of around 1.4%. So it really varies greatly for this clade, and we would expect the mortality rate to be lower within the US or other locations that have good health care systems.

The current outbreak in DRC (Democratic Republic of the Congo) for clade I has a case fatality rate of up to about 4.6%, and it is a select agent. So that's different than clade II, which is the monkeypox clade that was circulating, beginning in 2022, across the globe. We continue to see a case fatality rate of around 1% or less for clade II. Next slide.

All right. So clade I has previously been associated with non-sexual routes of transmission. Usually, it's associated with close household contact transmission, and this is primarily due to zoonotic transmission. So individuals are out capturing food in some food-insecure areas. They become infected. They bring that virus back, and then some of the household is also infected. So that's typically how we saw clade I transmitted.

In 2023, we saw a dramatic increase in the number of suspect cases. There were over 14,000 suspect cases and 660 deaths, and then in 2024-- this number needs to be updated-- but we've already seen over 1,000 cases, with 101 deaths. This is seen in 23 out of 26 provinces, as you can see in the picture on the right.

So almost the entire country of DRC is reporting suspect mpox cases, and I say "suspect," because most of them have not been tested by laboratory tests. They are only being called mpox based on the clinical presentation, and this is because DRC has very limited testing that is occurring. During 2023 only around 9% of all cases were tested. The other concerning flags we saw in 2023 is that there were cases in urban settings, where we typically haven't seen mpox and then also cases along borders, really raising some concerns about spread to other countries. Next slide.

So the transmission in DRC is quite different from what we see in the U.S. and also different from what we've historically seen in the DRC. And really, the main demographic group that's being infected in the DRC seems to be in children, and that's also where most deaths are occurring, and this is less than 15 years. So that is actually what we historically have seen, but we've also seen transmission due to sexual

contact and sex trade workers. Primarily, these are women sex trade workers, so not exactly the same outbreak setting that we saw start in 2022. But concerning, again, because we haven't seen sexual transmission of this clade in the past.

So I mentioned that only 9% of the specimens have been tested. And then we have seen some sequence data come out of the DRC that does continue to support that there are zoonotic introductions of this virus and not necessarily sustained human-to-human transmission occurring, but we are lacking a lot of information. This is a very limited number of specimens that are being sequenced.

And then I mentioned that we're seeing new provinces without a history of zoonotic transmission, including in sex trade workers, where there are cases of mpox occurring. Next slide. All right. So going into the U.S. preparedness, in case we do have a case of clade I. Next slide.

So today, there are still, thankfully, no cases of clade I mpox detected in the United States or anywhere outside of endemic countries within Africa. However, we are raising awareness about these concerning flags that I mentioned with these outbreaks in the DRC. And so to do this, we did issue a HAN in December, where we're encouraging clade-specific testing in DRC travelers.

We're encouraging vaccination, because right now, only one in four of eligible individuals within the U.S. have received a JYNNEOS vaccine, and the messaging that prevention on both vaccination and treatment are expected to perform similarly for clade I as we've seen for clade II. We also put out a travel health notice alerting about the outbreak in the DRC and increasing our clinical outreach, again, just to make sure clinicians are aware of this outbreak, are still looking for impacts. We're still having ongoing cases of clade II, and we want them to be aware of the possible cases from clade I from the DRC. Next slide.

So for diagnostic testing in the U.S., we do lean heavily on the non-variable orthopox (NVO) tests, which is the FDA-cleared tests that we used primarily during the 2022 outbreak. We have greater than 70,000 tests per week capacity. This test is FDA-approved, and it targets a conserved area of the monkeypox genome. So there's little risk of false negatives with that test due to mutations.

We have a strong performance history, and labs are familiar with it. And there's four commercial labs that are providing national coverage. Three of those are running the FDA-cleared NVO tests, and one is running a multiplex that targets both NVO and a clade tube target. We do believe that patient diagnosis and care management is best directed by the NVO tests, and that patient care does not change based on the clade. Next slide.

However, we do want to make sure that we have strong surveillance across the country to identify clade I cases, and so we continue to receive all NVO positives from our public health labs and some of the commercial labs using the NVO tests. We ask that all of those be sent to us, so that we can do our clade-specific PCR testing. We also do sequencing to look at mutations that could impact our medical

countermeasures, and it's important to note that, sometimes, we can't receive those under CLIA, but we do still test them for surveillance purposes, to make sure that we're only seeing clade II in the U.S.

There're also labs across the country that are performing other surveillance methods, such as sequencing of mpox positives, and also labs that are performing a clade II NVO multiplex. So I mentioned Quest, also many labs that are using Cepheid, which is an EUA-approved test that has a similar multiplex setup. So we just ask that those labs pay attention to those results, and if you have a positive NVO-negative clade II, that could be a mutation in that specimen, but it should be tested additionally to ensure it's not clade I. So we do ask labs to alert CDC in their jurisdiction, if they have a specimen with such a test result. We're also continuing to do wastewater testing and have switched our contracting company over to NVO to make sure we're not missing any mpox cases. Next slide.

So this last slide is just some information. If you need any assistance from us, we are happy to provide. So we did, during the last outbreak, share inactivation data for orthopoxviruses. We can do that again. If you need information about a specific buffer, please, reach out, and I can verify if we have that to share with you. That is for all orthopoxviruses, including clade I. Also, if there's any material we can transfer, if you're interested in bringing up a clade-specific test, inactivated virus, or different orthopox DNA, we've done that with some labs. So happy to do that after the tech transfer agreement is in place.

And then also sequencing, we have some genomics experts that are happy to weigh in on sequencing approaches to see if you can differentiate the clades, and if there's any other ways to support, just let us know. Next slide and think that's it. Happy to take questions.

Sean Courtney: All right. Thank you for that update, Christy. Really appreciate it. There is one question right now, and it is, can mpox be considered as an opportunistic infection among HIV-infected subjects?

Christy Hutson: Well, I'm not a clinical expert. So I'll just tell you my opinion, which is we do see, of course, with anyone with immunocompromised status. So during the 2022 outbreak, those with uncontrolled HIV that have a poor prognosis and generally had more severe infections.

Those with well-controlled HIV actually tended to get over the infection just fine with supportive care, for the most part. Of course, there were exceptions. So I would say, like many other conditions, that could lead to potentially being more susceptible to an infection, if you are immunocompromised, but it really depends on that individual person's health status. So I would not say that that would happen for every individual with HIV, but again, not a clinical expert there.

Sean Courtney: Great. Thank you. Appreciate that. A couple other questions have come in. Let me get through this first one. So one question is, do you know of any commercial labs offering testing for clade I?

Christy Hutson: So there is no commercial labs that we're aware of offering clade I testing, but as I mentioned, Quest is one commercial lab that offers a multiplex that looks for clade II and orthopox generic target. So we can use that. If you have an orthopox-positive, clade II-negative, that should be

treated as high suspicion for clade I. It could be a mutation, but we definitely want to do additional testing to confirm. So although it's not specifically clade I testing, it very much helps us under those surveillance efforts to see if we have any clade I circulating.

Sean Courtney: OK. Great. Thank you. Another question and, again, realizing that you are not a clinician. But it's around what the treatment plans are, if you're aware of that, or maybe you can even just say if there's differences between a clade I versus a clade II infection treatment options or vaccine options.

Christy Hutson: So it's exactly the same medical countermeasure. It's the same vaccine for clade I and clade II, the same treatment for clade I and clade II. There might be a lower bar for starting treatment for clade I infections in certain individuals, but again, we really want to make sure treatment is based on that clinical picture.

We have seen resistance occur against TPOXX and so we don't want to indiscriminately use. It should be based on the vaccine status of the individual, their immunocompromised status, if they have one, et cetera. It shouldn't be given just to anyone with clade I. So same medical countermeasures for both clades, potentially slightly lower bar of starting TPOXX treatment for some individuals with clade I.

Sean Courtney: Perfect. Thank you. Another question, I think I can answer this, but I'll turn it to you is, what type of BSL setting do you know these tests are being run in? Like our laboratory is running them in BSL-2's or what?

Christy Hutson: Thanks for that question. So one of our goals with providing the inactivation data was to help labs make that decision. Monkeypox virus, when you're culturing it and things, is listed as a Risk Group III pathogen. If you look at the BMBL, it's actually recommended that, for vaccinated individuals, they can do that in a BSL-2 setting for in vitro work with monkeypox virus.

But again, when we're thinking about our clinical laboratories that are doing diagnostic testing, that's not quite the same risk group as those that are culturing the virus. So we do have that inactivation data to help labs determine what biosafety level they can work safely with those samples, so they know exactly when it's inactivated, and we can provide that. But many labs are working in biosafety level two, especially if they are vaccinated, but it very much should be based on your individual risk assessment. But Sean, please, add any other information there, if I didn't cover it.

Sean Courtney: Oh, no. That's great. I appreciate that update, and that actually kind of leads into our next speaker. And I don't have any other questions right now, so I just want to say thank you for joining. I know you have to drop-- of course, one came in. Sorry, before you leave, I'm going to ask one more. Oh, let's get through it real quick. So it says, if clade I begins circulating in the U.S. with any type of incidence, how will that impact viral cultures being done in the labs? It says we continue to inadvertently grow clade II virus in cultures, because physicians do not suspect this.

Christy Hutson: That is a really interesting question, and I've actually not heard that feedback. So we have been working with our DOT and other colleagues to treat waste and specimens from clade I cases, as category B. We're very optimistic that we will get that enacted, but it's still going to be a select agent. So viral cultures will still have to be shipped with category A, for instance. I see Shaw is on, so he can add here from select agent regulations. But that lab will still have to report that virus, make sure it's secure, and then either destroy it or ship it. So I think that, regardless of if they've cultured it or not, Shaw, it would be the same, but please, add anything that I have left off.

Shaw Gargis: Yeah. That is correct, and so if you-- the same with any other select agent. So after the point of identification, then once it's identified as a select agent, then it just must be destroyed or transferred within seven days after identification.

Sean Courtney: All right. Well, thank you both, and then, Shaw, I'm going to keep you up then so. Thank you, Christy, for joining today. If we get any additional ones, I'll send them your way. But yeah, so with that, let's introduce Shaw, who's here now. Shaw, is with CDC's Division of Regulatory Science and Compliance, and he's going to give us an update on mpox reporting. So I will turn it over to you, Shaw.

Shaw Gargis: Yeah. Good afternoon. Thanks for letting me join the call today. So mostly, I'm going to be focusing on mpox virus and the Federal Select Agent Program regulations. Christy touched on some of this, but I'm going to go into a little bit more detail about when the regulations would apply, if we were to say in pox clade I in the United States. So next slide, please.

So in 42 CFR 73.3, under the HHS select agents and toxins, we list, as one of our HHS select agents, is monkeypox virus or mpox. So an HHS select agents or toxins that meet any of the following criteria are excluded from this part. So we have a subsequent exclusion in our regulations that say, if there's the West African clade or, as Christy was talking about, clade II of mpox virus, then that is excluded from the regulations. However, you see that it's, mpox virus is a select agent. mpox clade I is a select agent, and you have to show that it is mpox clade II for it to be excluded from the regulations. Next slide, please.

So there are the two clades of mpox virus, the Congo Basin, clade I, or the West African clade, which is clades IIa and IIb. IIb being the one associated with the 2022 U.S. outbreak, and all indication was that it was associated with that clade. We did not receive any notification, as Christy said, of clade I in the United States. So mpox virus is regulated as an HHS-only select agent, and it needs that possess user transfer, this agent must comply with the select agent regulations, unless there is an exemption, applicable exemption or exclusion, and I can get into those. Next slide, please.

So one of our exemptions that would really apply in this setting is the diagnostic specimen exemption. So clinical or diagnostic laboratories or any entities that possess user transfer an HHS select agent contained in a specimen presenting for a diagnosis or verification is exempt from the requirements of the select agent regulations, if after the point of identification, that report of identification is sent to the Federal Select Agent Program. During the point of possession by the non-registered entity or non-registered

clinical or diagnostic laboratory that, select agent is secured from any potential theft, loss, or release. And then the material is transferred or destroyed in accordance with the parts of the exemption.

So if it is a known select agent, then it must be shipped with what's called a form two, which is the authorization for shipment, if you were to say send it to another laboratory for additional testing or for reference laboratory testing or something like that. But it's after the point of identification that it then becomes a select agent, and then the applicability of the regulations apply. When you're talking about the exemption, so this exemption would apply to material that has been identified as being or containing the mpox virus.

So if the clade has not been determined by the assay, then it is a select agent. Or if the clade has been identified as the Congo Basin or clade I, it is a select agent. But if the assay does not-- or identifies as clade II, then that is excluded from the regulations. Next slide, and I'm going in a little more detail on that.

So an entity may retain identified material, if they're registered with the Federal Select Agent Program and are also approved to possess mpox virus. And the Federal Select Agent Program regulates material that has been identified as being or containing a select agent. However, one thing I do want to point out here is that identifications of orthopoxvirus, or the NVO assay, are presumptive identifications for mpox virus and are not considered select agents by the Federal Select Agent Program until identified as being mpox virus or another select agent. So the point here is orthopoxvirus is a presumptive identification and, therefore, is not an actual identification of mpox virus. Next slide, please.

So we've broken it down here in a table to say when a specimen would be subject to the select agent regulations. If you do the NVO or non-variola orthopox assay, if it's positive for that, then it is not subject to the select agent regulations, because it has not been identified as mpox. If you're running a mpox clade undetermined, or such as a generic mpox assay, then yes, that material would be subject to the select agent regulations, because our list includes the agent mpox on the list.

And then goes for mpox virus clade I, that is a select agent. So yes, at that point of identification, if you were running a clade-specific diagnostic assay, then if it showed up as clade I, yes, that is reportable and is subject to the select agent requirements. But if it's in mpox virus clade II, if you're running an assay, as I think Christy said, some entities are running like an NVO and clade II assay, or even just like a clade II-specific assay, then if it is identified as clade II, then that is excluded from the regulations and not subject to the requirements. Next slide, please.

So with that, I'll take any questions. I do want to mention, during the 2022 U.S. mpox outbreak, we did allow for a delay in reporting, which is we allowed for up to 180 days of reporting. Say if you did like an mpox generic assay, and that is required to be reported, since that is considered an mpox.

So we did review receive a few reports of those, but we did allow for a delay in reporting, so there wasn't that reporting burden on laboratories. Right now, that is not in place for mpox clade I in the United States, and it's also expired for the 2022 clade II outbreak. But if we saw cases in the United States, it may be

something we could consider, and we can provide additional information. So if you have any questions, please, see our website or our email address, and we'll be glad to help clarify any questions you have.

Sean Courtney: All right. Thank you for that, Shaw. So just to follow up on what you just said here at the end, so you said that extension used to be 180 days. What is the-- it's back on its original--

Shaw Gargis: Back on seven days now. So you have seven days to report the identification of mpox.

Sean Courtney: Perfect. Thank you, and I do not see any questions right now. But I do want to say thank you for joining our call today and providing this update. If you can hang out online for the rest of the call, if any questions pop up in the Q&A function, if you could just answer them within that function, that would be great. If not, if we receive email addresses, we can follow up with you as well outside of this, but again, thank you for joining our call, and—

Actually, see, it's happened again. One popped up. So just one second here. So it says, if your lab runs a clade II-specific LDT, and it is NVO positive but clade II negative, would that be considered a select agent?

Shaw Gargis: No. So since it's a positive for the non-variola orthopox assay, that is not an identification of mpox. Since it's a presumptive identification for mpox, it's not an identification of mpox, and it's a non-variola orthopox identification. Therefore, that would not be subject to the select agent regulations.

Sean Courtney: OK. Great. Thank you for that clarification. Appreciate that. Great. Well, we can try this again. So again, thank you for joining, but if any of them pop up, please, jump in there and give us a hand in responding to those. But as always, really appreciate you joining our call and providing this information. So thanks, Shaw.

Shaw Gargis: No problem.

Sean Courtney: All right, and we're going to shift gears a little bit. For our last presenter, we have Anastasia Lambrou from CDC's Coronavirus and Other Respiratory Viruses Division, and she's going to discuss early detection and surveillance of the SARS-CoV-2 variant BA.2.8-- excuse, me BA.2.86. Anastasia?

Anastasia Lambrou: Yeah. All the variants have fun names. Right? But hi, everyone. Thanks for having me today.

I'm representing the team shown on the slide here, and I'll be presenting a quick overview of our MMWR titled "Early Detection and Surveillance of the SARS-CoV-2 Variant BA.2.86 between July and October 2023." Next slide, please.

So I'll start a bit with some background on the variant itself and then work through our methods, results, and end on how our approach impacted public health action, as well as some implications for future preparedness as well. Next slide, please.

Starting with some background, in this MMWR, we outlined how we at CDC used a multi-component surveillance approach to track and monitor the SARS-CoV-2 variant BA.2.86. These surveillance components included the national SARS-CoV-2 genomic surveillance from case specimens, the traveler-based genomic surveillance system from travelers, national wastewater surveillance from wastewater, as well as this last category here, digital public health surveillance, which included public genomic data repositories, news and social media. And each of these early detection components shown here had some kind of genomic surveillance or sequencing component. Next slide, please.

So you might remember back to August 2023, but this is when the BA.2.86 variant was first detected, reported, and the global genomic surveillance and public health community really raised the alarm for more enhanced monitoring. Because this BA.2.86 variant had greater than 30 mutations in its spike protein, compared to other circulating variants at that time, so it further emphasized this need for tracking and evaluating its full public health impact at that time. Next slide, please.

So MMWR study had three major objectives. First, let's describe how we use these multi-component surveillance approaches at CDC in genomic sequencing in real time to assess the risk of these variants, outline the early detections of BA.2.86 and what mechanisms we used for that, and then lastly, to look at also the global spread of the BA.2.86 variant. Next slide, please.

So now, diving into the methods for our objectives. As I mentioned at the start, this MMWR outlines our multi-component surveillance approach that we use to detect BA.2.86 and track its early emergence. So here are those four major components again, and you can think of these components like different layers of early warning to track and find this variant. These are deployed in different populations at different levels. So starting with the national SARS-CoV-2 genomic surveillance, this is from multiple sources, inpatient, outpatient, of U.S. human respiratory virus specimens that are sequenced at CDC and also commercial labs and other sources.

Next is traveler-based genomic surveillance. This is a sampling of travelers from six major international airports in the U.S. Next is the National Wastewater Surveillance System. So now, here's one of our environmental layers, looking at wastewater. That currently services 40% of the U.S. population.

And lastly, the digital public health surveillance component, looking at those global repositories, like NCBI and GISAID, as well as news media, social media, and some global events-based surveillance. This became really important for us, because some governments and countries actually only posted first cases on social media, like X, like in Denmark. So we really wanted to monitor all of these layers in tandem. Next slide, please.

So our team would confirm and pull this data from different components and then analyze it through descriptive statistics, mapping, and synthesize these results from the four major components and look at real time risk analysis. In this MMWR, we also took a more in-depth, detailed look at the first two weeks of BA.2.86 emergence, looking at BA.2.86 as almost like a case study for these early warning layers. What components are detecting this variant, when, and how? Next slide, please.

So now, we'll jump into the results of our MMWR. So this is a timeline of those first two weeks that I mentioned, honing in on what happened during those early days. You can see the report date along the timeline and, on top, what surveillance component we used for those early findings.

So the first case was reported globally by Israel, and our team used digital public health surveillance to learn more. And then the first reported detections in the U.S. occurred four days later, on August 17, one through our national wastewater surveillance system use, in Ohio, and the second through a case-based respiratory genomic surveillance from Michigan. And just a few days later, traveler genomic surveillance program at CDC reported a BA.2.86 positive in a participant that was traveling back to the U.S. from Japan.

And then notably, at the end of this timeline here, I really wanted to include this date, because Ohio reported a case from a patient sample that was collected back at the end of July. And this patient is actually in the same area as the first wastewater detection that was reported nine days earlier. So this further highlights how these different early detection layers complement one another, and also how wastewater here served as a really early indicator for this variant. Next slide, please.

So our CDC team did not only monitor the BA.2.86 emergence in the U.S., but we also took a global perspective through the digital public health surveillance. Here, you can see two side by side maps, the first from August 26 and the second from October 23, to really illustrate the global rapid emergence of the BA.2.86 variant. So looking back at the end of August, detected in seven countries, reported from them, and then at the end of October, up to at least 32 countries across five continents.

So we really wanted to continue to monitor and work with global partners, and a lot of our global partners also have these multi-component systems. So it was important to not only look at the respiratory specimen side but also global wastewater as well. Next slide, please.

Now, I'm looking at time between human specimen collection and report in public databases. And we included this in our MMWR, because decreasing that time between specimen collection and sequence report is really critical for early public health action. So we plotted and measured the time between specimen collection and reporting from data in the large global public repository GISAID. This did not include wastewater detects, but the median lag time we found in this early period for BA.2.86 was 14 days, with a range of 5 to 29 days. Next slide, please.

We also included this dendrogram in our results to show how genetically different BA.2.86 was compared to the other SARS-CoV-2 variants that were circulating at that time and predominant. You can see

BA.2.86 in that blue box there, and below were the XBB sublineages that were circulating at the time, so very different and really critical to monitor. Next slide, please.

We also wanted to highlight that, even though this MMWR focused on BA.2.86, this same multi-component surveillance approach is used for other SARS-CoV-2 variants and was really important for us to maintain during that time, as JN.1 emerged. JN.1 is a sublineage of BA.2.86, and it rapidly rose to predominance. Next slide, please.

Taking a deeper look into JN.1 and bringing us also to present day, JN.1 accounted for approximately 94.9% to 97.4% of circulating variants for the week ending February 17. You can still see in that box there that BA.2.86, that parent, is still circulating-- that we monitored in our MMWR-- but at very low levels. And JN.1 has really taken over in the U.S. and globally. Next slide, please.

So how did we use these results for public health response? So our multi-component approach led to rapid risk communications, further laboratory characterization, as well as public health coordination. So we had weekly respiratory virus updates that came out of CDC and debriefs with our STLT partners, lab partners, CST, and others. Early detection and coordination really fostered collaboration between sequencing labs and CDC.

We were sent residual samples to CDC for isolation, early characterization, and also neutralization studies, to really better understand if this variant had a potential for immune escape and how severe. Some high-quality sequences that were also generated were used at CDC for further understanding its geographic distribution and growth and really aided in lab based and computer-based studies and simulations to look at immune escape even further. These different surveillance components at CDC that I discussed are also housed in different parts of CDC. So we really fostered strong collaboration to detect and characterize for public health risk assessment. Next slide, please.

I won't go over these in too much detail, due to time, but I wanted to show a few examples of our rapid risk communications that came from our investigation that was in the MMWR, and these are the CDC Respiratory Virus Updates. So if you think back to that timeline I showed, we reported our first case in the U.S. on August 17, and less than a week later, we put out our first update publicly on BA.2.86.

What do we know? What do we not know? Where is it spreading, and what are these key public health questions that we need to answer about this variant, moving forward? And these updates have continued as we've also seen new variants in the landscape. Next slide, please.

So in conclusion, despite decreases in SARS-CoV-2 sequencing, especially post the public health emergency, our genomic surveillance systems across those components detected BA.2.86, which was a novel lineage that circulated at very low levels, and yet we did pick it up across our components. Using this multiple surveillance system approach and integrating genomic sequencing was really successful for enhancing early detection and tracking and also helped us do some early characterization. And SARS-

CoV-2 variants will continue to emerge. It's really critical to monitor and keep these layers intact. Next slide, please.

We did have some limitations of our MMWR and analyzes, such as there are very levels of information and different levels of metadata completeness across these different layers, especially in the public digital data. Our digital public health surveillance component was also largely manual, apart from when we pulled down genomic surveillance data from large repositories. Global genomic surveillance is really limited by the lag time between specimen collection and reporting, as we discussed, especially for that real time actionability.

There's also lack of standardized methods for some genomic surveillance data in public repositories. And where do we put wastewater data, and how do we link it with clinical and other forms of genomic surveillance? And lastly, we had varied data quality, reporting, and aggregation standards across the layers to bring them together for synthesis. Next slide, please.

So thinking about implications for preparedness, our BA.2.86 MMWR was really this case study that highlighted the importance of using multi-component surveillance, monitoring different settings, populations, and interfaces. And with sustained resources, we can apply such an approach for early warning of known and even unknown novel public health threats. Next slide, please.

I just want to end looking towards the future. Public health surveillance and early warning can benefit from innovations in pathogen testing, including genomic sequencing, capacity building, as well as interoperable data reporting systems. Furthermore, thinking about public-private partnerships, automation, and other tools that can help us address these bottlenecks that we learned about across early detection and really decreasing those lag times. We've learned a lot from outlining and coordinating such a multi-component system, and it's really critical to continue to deploy such genomic surveillance systems to strengthen early warning, preparedness, and future response. So thank you.

Sean Courtney: All right. Thank you for that update and that presentation today, Anastasia. So I do not see any questions right now. So I'm just going to say thank you for presenting today and joining our call. It's very much appreciated. So thank you.

Anastasia Lambrou: Thanks for having me. Yeah. If you get any emails, we'll definitely respond to any questions that come in later on.

Sean Courtney: Absolutely. We will definitely share. So thank you so much. All right, and with that, I just want to say thank you again to all of our speakers today.

As a reminder, we typically hold these calls on the third Monday of each month, and they're scheduled for one hour. March's call is scheduled for March 18, from 3:00 to 4:00 PM Eastern time. Let us know if you have any suggestions for topics for future calls, as we look forward to continuing to discuss these hot topics and to answer any of your lab and testing community needs.

As mentioned at the start of this call, we'll try to get the audio, the transcript, and the slides from today's call posted on our website within the next two weeks. And you can find CDC on social media, on Facebook, Instagram, LinkedIn, X, formerly Twitter. So please, follow those to stay up to date with the latest news and any recommendations from CDC. And again, just thank you all for joining us today, and we continue to be grateful for your work. And we'll talk to you again on Monday, March 18. Take care. Bye.