Agenda
Laboratory Outreach Communication System (LOCS) Call
Monday, November 21, 2022, at 3:00 PM ET

- **Welcome**
  - Sean Courtney, CDC Division of Laboratory Systems
- **Domestic Preparedness for Sudan Virus Disease**
  - Joanna Prasher, CDC Uganda Ebola Outbreak Response
- **Sysmex Hematology Portfolio and High-Risk Sample Processing**
  - Andy Hay, Sysmex America, Inc.
- **Efficacy of Ebola Inactivation Methods**
  - Ninecia Scott and Brian Harcourt, CDC Division of High-Consequence Pathogens and Pathology
- **SARS-CoV-2 Antigen Testing Guidance Update**
  - Muktha Natrajan, CDC Division of Laboratory Systems
- **Diagnostic Influenza Testing for the 2023 Influenza Season**
  - John Barnes, CDC Influenza Division

SEAN COURTNEY: All right. Good afternoon, everybody. My name is Sean Courtney. I'm a Health Scientist in CDC's Division of Laboratory Systems (DLS). And on the screen, you can see the agenda for today's call. We're covering a couple of different topics today going from the Ebola outbreak in Uganda, some COVID guidance updates, as well as some flu diagnostic testing updates. So we'll go ahead and get started.

So as you've 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 we've been hosting these calls since March of 2020. So DLS supports this work across four goal areas. So we have quality, workforce and training, preparedness and response, and informatics and data science.

And so as always, we'll be sharing the information transcripts and audio recordings from today's call on our LOCS web page, which is shown here on the screen. So that if you miss anything, or need to go back, those resources will hopefully be available within the next couple of weeks. As always, we'll be holding our next call in December. So we have these on the third Monday of each month. So this is going to be on Monday, December 19 from 3:00 to 4:00 PM.

And so our Training and Workforce Development Branch wants to hear from you. So if you have any questions, or concerns, or gaps within education or training, we would like you to please contact them at labtrainingneeds@cdc.gov. And if you have a question today, we'd like you to please use the Q&A button within the Zoom webinar system. Please do not use the chat function. We also would like you to please include your email address in case we are not able to answer your question during the call, or if we need

to submit that question to a different SME (subject-matter expert) during today's call. So please use the Q&A function instead of the chat feature.

And as always, slide decks may contain presentation material from panelists who are not affiliated with CDC. And so presentation content from external panelists may not necessarily be CDC's official position on the topics covered. And with that, I'm going to go ahead and get started and turn it over to Joanna Prasher, who's going to be discussing the domestic preparedness for Sudan virus disease. Joanna?

JOANNA PRASHER: Thank you very much, Sean. And good afternoon. I am currently serving as the lead for CDC's Domestic Preparedness and Response Task Force within CDC's Ebola outbreak response. So I'm just going to spend a couple of minutes with you today giving you some basics on how that outbreak is going in Uganda, but spend most of the time this morning talking about the efforts we're undergoing, and working with our interagency, and our state and local partners to make sure that we are domestically prepared should there be a case of Sudan virus disease (SVD) in the United States.

So as of a couple of days ago, which is the latest information that I have, there was a total of 141 confirmed cases reported across nine districts in Uganda. The CDC Country Office in the area has deployed 10 full time staff who are working to support the government of Uganda and the Ministry of Health in that response. And we've also deployed CDC responders from HQ as well.

But to be clear, that as of right now, there are no probable or confirmed cases of Ebola in the current outbreak outside of countries other than Uganda. The risk of Ebola in the United States does remain low. However, that being said, CDC is working as I said, with our interagency and our state and local partners to make sure we are ready should there be a case present here in the United States.

So I'm going to highlight a couple of avenues of work. First, I think folks are probably very much aware that the Department of Homeland Security has started funneling passengers from Uganda to five US airports, that's Atlanta, Chicago, Newark, New York City, and Washington Dulles, to help facilitate health screening of incoming travelers to the United States who have been in Uganda within the past 21 days. To date, so that's through the 20th of November, CDC has screened 4,816 persons at these funneling airports, 69 required what are called secondary public health assessments, but none have been referred to hospital, and there have been no high-risk exposures identified through this process.

CDC has been sending health information alert text messages to travelers that are arriving from Uganda. The messages ask travelers to monitor themselves for signs and symptoms, and to provide information of what they should do if they get sick, specifically, to isolate, call the public health department, and share their travel history with their doctor. To date, that's through the 17th of this month, we've utilized what's called the CDC Text Illness Monitoring, or TIM system, to send general health text messages to 2,790 unique phone numbers of arriving international travelers from Uganda.

We then have been supporting US health departments by sharing contact information for these travelers so that health departments can conduct follow-up risk assessment and management of travelers following

CDC guidance. During the week of the 6th to the 12th of November, jurisdictions were monitoring 1,160 travelers to give you some sense of the level of effort going on nationally here. To support that follow-up, we've also started with the help of the CDC Foundation distributing cell phones to travelers from Uganda who arrive without a cell phone or a US cell phone service, or US phone number. This supports local and state health departments contacting these travelers to do that important follow-up. To date, we've distributed over 240 cell phones to such travelers.

And the past couple of weeks we brought online a REDCap based system to collect information from our state and local partners so that we can monitor how the monitoring is going of the travelers, and figure out if there's anything else that we can do to continue to assist that effort. If jurisdictions were to have someone for whom Ebola is a concern, CDC strongly recommends consultation with CDC prior to testing. State and local health departments can contact CDC's Viral Special Pathogens Branch by calling CDC's Emergency Operations Center at 770-488-7100, and requesting on call epidemiologist.

As of this weekend, we have conducted 29 of such Ebola related clinical consultations since the start of the response on September 20. Only one to date has been referred for Ebola testing in consultation with the jurisdiction and the treating health care facility. That person, I'm happy to say tested negative.
I note this group is very much aware, but I will also note that we have also been working to increase the ability to test for Sudan virus domestically. As of now, I'm very pleased to say that 28 Laboratory Response Network (LRN) labs can use the DOD (Department of Defense) developed and FDA (US Food and Drug Administration) cleared BioFire Warrior panel to test for Sudan virus under CLIA regulations. We're also collaborating with our ASPR and DOD partners to implement this testing with the Warrior panel in all 10 of the regional emerging special pathogen treatment centers, one of which is located in each of the 10 HHS regions.

We are also on November 4th, earlier this month, we put out a specimen referral guidance to all of our laboratory health department and clinical community partners to ensure that all jurisdictions as of today should know where they can send specimens for SVD testing should that become necessary. And of course, CDC has in-house diagnostic assay for confirmatory testing in case of a presumptive positive from an LRN laboratory. We are also working with our state and local health departments, specifically starting with those jurisdictions that are either in the surrounding areas around the funneling airports, or what we call the priority jurisdictions that have been identified because they have the preponderance of returning travelers from Uganda, or are the site of people who self-identify as part of the Ugandan diaspora here in the United States.

We have completed outreach and technical assistance sessions with all of these jurisdictions talking about their plans for improving readiness for the response, including health care system readiness, EMS readiness, and testing protocols. We've walked them through three specific scenarios to help us all better understand how such suspect cases might present in jurisdictions. It could be either a suspect case identified at a funneling airport, a suspect case identified during state monitoring of return of travelers from Uganda, or a case presenting for care at a frontline hospital. And this has really provided an

opportunity for us to learn about jurisdictions plans, and identifying any areas where we or our federal partners could offer technical or other assistance.

Finally, should there be a domestic Ebola case, CDC has pre-rostered multidisciplinary CDC Ebola response teams that jurisdictions can request to support public health actions that might be needed in helping health department to support the care and management of such a patient. We've also done a number of communication outreaches. So you may have seen on October 6th and November 7th we separately issued a Health Alert Network, or HAN, advisories for health care providers and health departments to increase awareness about Ebola, and include a description of CDC recommendations for case identification, testing, and treatment. And we are continuing to release regularly key messages to all of our STLT (state, tribal, local, or territorial) partners. With that, I will close, and turn it back over to you, Sean, or happy to answer questions.

SEAN COURTNEY: OK. Thank you so much, Joanna. I really appreciate today's update. We do have a couple of quick questions. And I know that some of them were being answered in the chat. So I'll just go to this first one. It says, how quickly do samples need to be frozen after collection, prior to testing at CDC? Not all of our partners have the ability to ship on dry ice.

JOANNA PRASHER: Yep, understand. And I know that some of our laboratory specialists were not available unfortunately, this week. So yes, that looks like there might be someone who can address that. So I'll let maybe the person who addressed it in the chat, or we can circle back.

SEAN COURTNEY: Sorry about that. I think we'll try to take care of that within the chat like you mentioned. And the next question is, did you say that sentinel labs could use the BioFire Warrior panel?

JOANNA PRASHER: So there are at this point, 28 Laboratory Response Network labs that can use the BioFire Warrior panel, as well as I think at this point, six of the regional RESPTCs (US Regional Emerging Special Pathogen Treatment Centers) that we're working with ASPR (Administration for Strategic Preparedness and Response) and DOD. And I know there's interest more broadly that we're hoping to expand that access as well, working closely in partnership with DOD who manages access to that test.

SEAN COURTNEY: All right. Thank you for that. I do not see any additional questions at this time. But first, I'd like to really thank you for joining our call today. But if any additional questions do come up in the chat, we'd like you if you're available, to please hang around and answer those within the chat, that'd be great. We really appreciate it.

JOANNA PRASHER: I'd be happy to.

SEAN COURTNEY: Otherwise, Thank you so much. Again, really appreciate you taking time to present this to us today. All right, and so moving to our next presenter, we have Andy Hay with Sysmex. And Andy, I am going to stop sharing my slides, so that I can let you present yours.

ANDY HAY: Thank you, thank you, Sean. Just give me one second, everybody, just to pull up the slides. If somebody would be kind enough to tell me if you can see them, that would be appreciated.

SEAN COURTNEY: Yes, we can see them. Thank you.

ANDY HAY: Thank you. So good afternoon, everybody. My name is Andy Hay. I'm the CEO of Sysmex America. Thanks very much to the CDC for giving us the opportunity just to quickly provide all of you with an overview of our hematology testing portfolio, and our version of how high-risk samples can be processed, including Ebola samples.

Sysmex does have a comprehensive portfolio of hematology instruments, CVC counters. You can see them ranging top row left to right in terms of smaller clinic type systems, small hospital systems in the center, and then across the bottom row, a whole series of configurations all based on the same basic platform, which is known as the XN-1000 platform. And that can be presented in a number of different formats.

Just to give you an idea of those sort of configurations that are available, there's a short video. There's no sound to this video in case anybody's wondering where the sound is. So typically, a hospital would have two systems side-by-side, but they may also just have one in a smaller location. They could add to that system to include a Slidemaker Stainer on an integrated platform, or indeed, a digital morphology cell-imaging system. And the systems are somewhat infinitely configurable. They can be expanded.

And there's a generic term known as an XN-9000, or an XN-9100 that many of you have heard of from the 2014 Ebola outbreak. This is really just a configuration of XN-1000s Slidemaker Stainers and digital imaging systems all put together on an automated track. So essentially, all of these behave in exactly the same way. And in fact, if we look to some of the larger reference labs, there could be anything up to 40 or 50 of these instruments all together in one location, but they're all essentially multiples of the same theme of the XN-1000, which is a closed tube fully automated CBC system, and it's found in about somewhere in excess of eight out of 10 hospitals in the US would have this system.

So as we look across our portfolio, there's some definite no’s that we would not recommend be used in any kind of high-risk situation. I also want to draw your attention through these exclamation marks to some of the standalone digital morphology systems. And I'm going to come back to each of these. But generally speaking, unless they've got a stop or a caution sign against them, all of these we believe are suitable for use within a high-risk environment, and suitable for use with patients known or suspected to have Ebola.

If we go through each of the stop signs, the first one is an instrument called the Sysmex XW-100. And that's a CLIA waived hematology testing system. It's designed to be used outside of the normal moderately complex lab environment. And its clearance with the FDA has some very strong restrictions associated with it, including that it should not be used with any kind of known clinical abnormality, critically

ill patients, or any children. So in our opinion, even though this is a closed tube sampling system, this is not a suitable device for use in any kind of testing of a high-risk samples.

We also have two systems listed here below, the XP-300, and the XN-L 350, both of which are open tube sampling only. In other words, you have to pop the top off the vacutainer, or whatever closed tube sampling system is in use in order to aspirate the sample. That is seen to be an unnecessary risk when virtually, every hospital environment has closed tube sampling. So again, Sysmex would not recommend the use of their open tube sampling systems for this purpose. They have other uses and applications, but this would not be one of them.

There's also a number of Cellavision manufactured, sold, and distributed, and supported by Sysmex digital morphology systems. These standalone units you can see on the left here, require the manufacture of a manual blood smear. So their input is a spread blood smear onto the glass. And that in themselves, they could be used, as long as the smear had been prepared in a reasonable manner using recommended precautions and fixed.

But they're not necessary in as much as there is an integrated version of these units available on the larger configurations, which would mean that that aspiration of the sample and the spreading of the smear could be done automatically and would not need to be performed offline by opening the tube itself. Closed tube sampling is the solution to most of these management and most of these risk samples. So there is a smear and morphology system available integrated, but in the event that a lab doesn't have one of those, they could use these tabletop configurations as long as the blood smear itself had been prepared in a manner that's according to the guidelines. I'm going to stay away from what those guidelines are. I'm only here today and qualified to talk about the equipment that we provide and support.

There's also a smaller instrument that may be familiar to some of you, called the Point of Care Hematology Instrument 100, or PocHi-100. During the 2013-2014 outbreak, many hospitals acquired these systems and installed them inside biosafety level 2, or biosafety level 3 environments. That decision, or that recommendation to install them in that environment did not come from Sysmex. And because this is a closed tube system, Sysmex does not believe that there's any additional safety associated with putting a small portable system like this inside a biosafety lab.

In fact, we would recommend that the sample itself be handled in the central lab in the normal way. There's also a problem with servicing this unit if it's gone into a biosafety level 3 environment. Our service engineers may not enter to carry out any form of service. And the typical, normal service method for this instrument in the market is a return to base service where the instrument goes out of the lab decontaminated, and out of the lab into the hands of the carrier FedEx, UPS, or somebody, and then return to our service depot for repair, and then return back using the carrier to the lab.

We did experience major problems with carriers accepting products during the course of the last outbreak. And Sysmex overall, does not see any advantage, and doesn't recommend the installation of the small Point of Care Hematology Instruments into a biosafety level 2 or 3 environment. In fact, we

recommend that the Ebola samples known or suspected be treated in the same way as any other lab high risk sample.

So we do have a complete range of hematology testing solutions with all with closed tube sampling that are able to handle high risk samples as part of standard practice. Every customer of ours today would handle hepatitis, HIV, and all the other known risks in the same way as they should handle all samples as if they were high risk. So the configurations, the naming of the instrument, we're going to work with the CDC hopefully to get all of that cleared up and put the right instrument names and the right configurations onto the CDC website, and also update our technical staff so that if any of the customers, hematology labs phone in for advice, that they would get the same consistent messaging across all points of contact. We also intend to put out a customer bulletin with the same kind of Q&A shortly. So with that, I'm going to stop sharing, and Sean, I'm going to hand it back to you.

SEAN COURTNEY: All right. Thank you so much for that, Andy. Really appreciate you going over that with us today. There were a couple of questions. I'll just hand them over to you. The first one is, is the Sysmex information and slide deck directly available from Sysmex? And if so, do you have an idea of when that could be available?

ANDY HAY: Yeah, what I'd like to do is to create this customer bulletin containing the same information, and we would send that out to all of this, as many hematology customers as soon as possible.

SEAN COURTNEY: Thank you. Really appreciate that. The next question was, do the Sysmex XN-L 430, 450, 530, and 550 carry the Sysmex recommended status for high consequence testing?

ANDY HAY: The 430 and the 530, to 450 and the 550 all have closed tube sampling, so yes.

SEAN COURTNEY: All right. Thank you, just one second.

ANDY HAY: That's a very specific question, but yes.

SEAN COURTNEY: All right, thank you. All right. The next question I see is for pediatric patients, where a specimen is collected via finger or heel stick in a bullet microtainer, what hemanalysis options are available, as those are typically analyzed in open?

ANDY HAY: Yeah, that's a great question. From our perspective, we can't make a recommendation on how open tube samples could be handled. There is no good safe recommendation from the Sysmex perspective. The best I would suggest is that rather than collecting into open tubes, that the small pediatric closed tubes are used, which are compatible with the cap placing system.

SEAN COURTNEY: Great, thanks for that explanation. So I do not see any additional questions at this time. So I'm going to go ahead and thank you again for presenting today.

ANDY HAY: My pleasure.

SEAN COURTNEY: Yes, thank you so much. And if any questions do appear if you're able to hang around and answer them in the chat, that would be very helpful. And so with that, I'm going to go ahead and get back started sharing my screen here. Just one second. And move to our next presenter. We have Ninecia Scott, who is with CDC's Division of High Consequence Pathogens. She's going to talk about the efficacy of Ebola inactivation methods. Ninecia, are you here?

NINECIA SCOTT: Yes, I'm here. Can everybody hear me?

SEAN COURTNEY: Yes, thank you.

NINECIA SCOTT: Awesome. Good afternoon, everyone. So as stated, we'll be talking about the efficacy of bleach, or sodium hypochlorite and Micro-Chem Plus in inactivating Ebola. I'm Ninecia Scott once again, and I'll be delivering this information along with Brian Harcourt, who is the Biosafety Team Lead for Viral Special Pathogens Branch in the point of context here. Next slide, please.

So here, we have different classes of microorganisms that are ranked from most susceptible to disinfectants, which is in green and at the top, and the hardier pathogens that are least susceptible and harder to disinfect at the bottom, which are in red. So concentrations of 1.5% Micro-Chem Plus, a disinfectant that we use in all US level 4 labs, in 0.82% sodium hypochlorite, which is the equivalent of 1:10 dilution of household bleach, can be used to inactivate an enveloped viruses, bacteria, fungi, and non-enveloped viruses.

This concentration of 0.82 sodium hypochlorite is also able to inactivate much hardier pathogens, such as mycobacterium, and bacterial spores as well. Influenza, coronaviruses, such as SARS-CoV-2, as well as other bloodborne pathogens like hepatitis B and HIV, which are commonly seen in clinical labs every day are classified as enveloped viruses. Enveloped viruses, including Ebola viruses are the most susceptible types of pathogens to disinfectant. Next slide, please.

Currently, there are two concentrations of sodium hypochlorite that have been used for decades in ETUs or Ebola treatment units. So 0.5% is used to disinfect most non-living items, and this can include corpses, contaminated surfaces, bodily fluids like vomit, diarrhea, blood, things like that. And the point 0.05% is used to disinfect living tissue and other chlorine sensitive materials. So that includes skin, exposed skin, linens, thermometers, things like that. And so this is a good time to also remind people that bleach dilutions should be prepared fresh daily. Next slide, please.

So here, we have a published figure by Cooke et. al., which demonstrated that when Ebola was present on stainless steel surfaces, or these steel coupons that had organic soil loads which contained Ebola BSA and mucin to mimic common clinical settings, they saw that 0.5%, which is in the blue line, and 1% sodium hypochlorite, which is in the orange line, sterilized and inactivated about seven logs of Ebola after five minutes of contact time. What's interesting to note too is that they also looked at 67% ethanol, which

is in red, and they saw that that also inactivated Ebola after five minutes of contact time. However, we don't use ethanol for inactivation.

So it should also be noted that this experiment used a specific strain of called Ebola called Ebola Makona, which is a species of Zaire Ebola virus. Regulatory agencies accept the inactivation data from one species within a virus family is applicable to all species within a viral family, which basically means that this data that we've shown here can be applied to Sudan Ebola virus. Next slide, please.

So here in this 2018 paper by Smith, et. al., they basically saw that in dried human whole blood, containing Ebola, 1% sodium hypochlorite did not as effectively inactivate Ebola. And so this is not really that surprising, because it's well known that chlorine compounds do not penetrate particulates. And so bearing this in mind, alternatives should be considered when disinfecting dried blood. Next slide, please.

So we're going to transition to talking about Micro-Chem Plus. So 5% Micro-Chem Plus is used in every United States BSL-4. The Division of Select Agents and Toxins, also known as DSAT, requires validation data that Micro-Chem Plus inactivates Ebola from each select agent lab. So our in-house studies have shown there's at least a six log decrease in Ebola after one minute in a one-to-one mix with 5% Micro-Chem Plus. And although the manufacturer recommends about 1.5% working concentration, we actually use it at 5% of Micro-Chem Plus with a contact time of three minutes in our BSL-3 to provide a margin of safety.

So when it comes to Micro-Chem Plus data, there's not actually a lot of published data showing Micro-Chem Plus inactivation data. However, this 2022 paper shows that Micro-Chem Plus at a concentration of 0.56% with 15 seconds of contact time inactivates greater than four logs of Ebola. In the table at the bottom, we see that similar to the hypochlorite data previously shown. 1.5% Micro-Chem Plus was not as effective in inactivating Ebola in dried human whole blood. Next slide, please.

So with that, I really would like to say and give you these key takeaways, so first of all, treat all samples the same, as if they contain a high-risk pathogen. Earlier we showed that Ebola viruses are enveloped viruses, and they're classified as the most susceptible type of viruses to disinfectants. Inactivation data for when Ebola virus is applicable to all members of the virus family, so this includes Ebola, Sudan, Marburg, et cetera. 1.5 to 1% sodium hypochlorite effectively inactivates viruses on stainless steel surfaces with a soil load.

1% sodium hypochlorite is not as effective at inactivating viruses in dried whole blood. 5% Micro-Chem Plus effectively inactivates Ebola viruses. 1.5% Micro-Chem Plus is not as effective at inactivating viruses in dried blood. So blood should be soaked off with disinfectant, or alternatives should be considered. And then finally, if you have instruments that need to be contaminated, please contact the manufacturer for instructions. And with that, we'll take any questions if there are any on the next slide. Thank you.

SEAN COURTNEY: All right. Thank you so much for sharing that with us today. I do not see any questions right now. So I will go ahead and ask you-- well, again, thank you for joining us, and for sharing

that presentation. And if you can hang around and answer any questions should any pop up in the chat, that'd be really helpful. But thank you again for joining our call today.

NINECIA SCOTT: Thank you.

SEAN COURTNEY: All right, and moving to our next one, we're going to shift gears a little bit. And we're going to go over to COVID, and we have an update from Muktha Natrajan, who is going to be talking about the new antigen testing guidance update. Muktha?

MUKTHA NATRAJAN: Thank you, Sean. Good afternoon, everyone. I'm Muktha Natrajan. And I'll be presenting an update on CDC's guidance for health care providers who perform antigen testing. Next slide, please.

So a little bit about this web page, this guidance web page was first created in August 2020, and is intended for health care professionals who order or perform antigen testing in laboratory settings, or at the point of care. It's also intended for laboratory and testing professionals, and public health practitioners who perform antigen testing and reporting in a laboratory setting. It focuses on the diagnosis of new infections, and is not meant to serve as self-testing guidance for the public. And while most, but not all self-tests or at home tests are antigen tests, the audience for these two guidance pages, this one, and that of the self-testing page, are very different.

At present, FDA has granted 51 emergency use authorizations for antigen tests that include laboratory based, or moderate to high complexity tests, point of care tests, and wave tests, and cell tests. Antigen tests have been widely used for diagnosis, screening, and surveillance, of SARS-CoV-2 across health settings, including hospitals, and physician's offices, and skilled nursing facilities. And so CDC is currently updating communications about testing, giving actionable information on testing decisions, and streamlining our existing content. Therefore, it's necessary for CDC to maintain and update this antigen testing guidance for health care providers. Next slide, please.

The need to update this instant testing guidance became clear as soon as FDA released their repeat testing guidance, and CDC updated its new goals for public testing guidance. To distinguish this page intended for health care providers and to align with CDC's shift to a more education focused on testing options, we've updated the name of the web page to specify considerations for health care providers, and revised the order of the table of content to focus on general considerations and interpreting antigen test results. We've also removed specific sections on serial testing, given the new guidance on repeat testing.

The previous web page can be seen on the right here with the updated title highlighted above. The table describing the differences between NAAT and antigen test was removed from this particular page, and has been linked out because this content (nucleic acid amplification test) is already available on the CDC overview of testing page. Excuse me, and that's also for health care providers. Now, CDC is moving toward discrete information on individual pages to reduce redundancy. And that's why this table was removed from this web page.

Additionally, considerations of exposure to COVID-19 or vaccination status when determining repeat testing for negative antigen test results were removed from our published algorithm. We've also made three principal content updates to this web page. The first is the change in the order of information on the page to focus on general guidance for antigen testing and interpretation of test results, along with the antigen testing algorithm on the page.

The next update addresses when to consider performing repeat testing, or other testing after an antigen test result in symptomatic and asymptomatic individuals. The guidance provides details on factors that affect pre-test probability, and also aligns with the new FDA guidance on repeat testing for negative antigen test results. The revised antigen testing algorithm also provides an overview of these updates in the text. Next slide, please. I'll go into a little bit more here.

So what you see on this slide is the new antigen testing algorithm for health care providers, and has been modified to reflect the updated FDA guidance on repeat testing and CDC's general updates to the testing guidance, as well as being more suitable for a standalone interpretation. For example, we know health care facilities print out this figure as a reference guide in clinics and other testing venues. So this version now includes more detail within the figure itself with a few simple footnotes.

The algorithm flows from symptom status at the top from asymptomatic to symptomatic, to then the test result of positive or negative, to recommend action along the bottom side. Color has been used to represent the level of caution, and this is similar to the previous version of this algorithm, to allow for testing result and testing situation. Given our current knowledge of antigen test performance, the figure suggests that a positive antigen test result does not need confirmation.

We've also added more detail on the need for repeat testing for all negative antigen test results, either by NAAT, or additional antigen testing based on FDA’s guidance for at least two tests for symptomatic individuals, and at least three tests for asymptomatic individuals. We've also added considerations for alternative diagnoses early on, as early diagnosis and treatment are important in preventing severe illness for many pathogens that cause acute febrile respiratory diseases. So the goal of this web page and algorithm update is to ensure that health care providers and testing professionals have a resource to aid in their interpretation of antigen test results, to know when and how to perform additional antigen testing, and to understand what level of caution to prescribe Thank you very much for your attention, and that completes my talk. I'm happy to take any questions at this time.

SEAN COURTNEY: All right. Thank you so much for that, Muktha. I really appreciate you joining us today. Looking through the Q&A, there are some questions, but unfortunately, they're not relevant to what you just presented today. So we would have to get a different SME to be able to cover and address those questions. So if you did ask those questions, could you please reply with your email so that we can maybe get with an SME and get back with you on those. But Muktha, I am not seeing any other questions. Oh, here, here's one that just came in right when I said that. So do antigen recommendations and algorithm apply to home testing?

MUKTHA NATRAJAN: So these considerations are only for health care providers. So if the home testing is then being-- if the results are being discussed with your health care provider, the health care provider may consider the situation of the individual with regards to their home testing results. But it's not for the interpretation of the public who are performing home testing.

SEAN COURTNEY: Great. Thank you for that. All right, so next question is so for symptomatic patients, the recommendation is for the patient to return to the doctor's office for repeat testing two times?

MUKTHA NATRAJAN: For a negative antigen test, this doesn't necessarily mean in-office repeat testing. They can perform an at home test under the guidance of their health care provider.

SEAN COURTNEY: All right. Thank you. Sorry about that. Next question is, what about the previously positive within the 31-to-90-day window? Do they need a serial repeat testing for negative results?

MUKTHA NATRAJAN: Previously, PCR positive within the last 90 days. Is that the question? Sorry, Sean, I'm trying to find it.

SEAN COURTNEY: They don't specify. They just say previously positive within the last 30 to 90 days.

MUKTHA NATRAJAN: I'll type my answer back to that question in just a minute. Sorry, I'm having trouble opening Q&A, but I'll reply to that one.

SEAN COURTNEY: It's no problem. I appreciate it. Next question is, when was the algorithm rolled out?

MUKTHA NATRAJAN: So these updates have been cleared by CDC. And we're just awaiting the actual web page rollout. We expect it any day now. It's not officially online yet though.

SEAN COURTNEY: Great. Thank you. Next question was, is this also for assisted living facilities?

MUKTHA NATRAJAN: No, this is specifically for the community setting. There is separate considerations and guidance related to congregate settings.

SEAN COURTNEY: All right. Great, thank you. I do not see any additional questions at this time. So again, I just want to thank you for joining us on today's call. And if you can hang out, and if you see any additional questions that pop up in the chat, just take care of those, and we'd really appreciate it. But thank you again for joining us today. And so with that, we're going to pivot again. We're going to move over to John Barnes with CDC's Influenza Division, who is going to be discussing diagnostic testing during this flu season. John?

JOHN BARNES: Thank you, Sean. So I just wanted to go over some of the recommendations as we are having as I'm sure everybody is aware, a very early and very robust influenza season at this point. Just

some reminders of diagnostic influenza testing that we're going through, and things to be on the lookout as we go for under the 2023 influenza season. Next slide, please.

So the CDC currently has for influenza testing a series of IVD (in vitro diagnostics) or EUA (emergency use authorization) cleared kits. We have the A/B typing kit and the flu SC2 multiplex kit. These are really our first line for influenza diagnosis, or SARS-2 diagnosis. These are just do you have influenza? Yes. What type is it, A or B, or do you also have SARS? And these can be used interchangeably.

The next kits that we have are A-subtyping kit and a B-lineage typing kit. And these are really determining if we have a seasonal influenza virus, or the viruses that cause the seasonal epidemics that we go through every year, versus a zoonotic virus. And for that, one of the targets that we have is really our pdmINFA target, which targets the NP (nucleoprotein) of swine viruses. So we can tell if we've ever gotten any swine exposure, or swine virus actually instead of a normal human seasonal epidemic virus. And so these are the next level of kits.

And then finally, we have our avian A/H5 subtyping kit and A/H7 subtyping kit. And these determine if they're or H5 or H7 avian viruses. And these usually come with a note that they should not be formed unless a patient meets clinical or epidemiologic criteria for testing of those suspect specimens. Next slide, please.

So we have this algorithm that I've shared multiple times before, and really which we have the A/B typing kit or the flu SC2 multiplex as our first line of testing. These can be used interchangeably, and really, they are the same exact targets in both assays, except for the addition of the SARS coronavirus target within the multiplex. These determine if it's influenza A or influenza B. And then we can go further to go down through the algorithm to define subtype or lineage type from then on. We're asking people to pay close attention to this, because we have seen quite a number of zoonotic viruses this year. And then this year, we also have a desire to find out if we see any influenza B Yamagata viruses in particular, as we've not seen that virus in several years. Next slide.

So pandemic threats, please be on the lookout for these atypical viruses. Globally, we've had a lot of circulation of a lot of different zoonotic viruses in avian and swine populations. And in the last two years, we've had quite a number of different zoonotic influenza subtypes that have been detected. And so please look out for any of those influenza A viruses that we cannot actually attain a subtype that has a influenza A target below 35, 35 or below, but lack reactivity for H1pdm09, or H3 subtypes as a diagnostic specimen to CDC. Please send those immediately.

As I mentioned, also, we're looking for these B Yamagata viruses. We have not seen those in the last couple of years. And most of the viruses that we have seen collected are actually LAIV cases where we have live attenuated influenza vaccine that has persisted a little bit too long in the nose, and we've gotten a swab of somebody who has been treated with that. And so be aware that this is also a possibility, and that we may be reaching out to you all if we have a B Yamagata potentially case, if there has been

exposure in the actually-- a live attenuated vaccine has been given, or there was somebody else in the household in which this has been given as well. Next slide.

Just to go over a couple of results for some of the diagnostic viruses for variant viruses to be on the lookout. We had a fairly robust zoonotic season, particularly in swine influenza this year. And we see some differences in the way that the testing actually displays itself when we have some of these clades of swine in humans, causing human infections. So if you look at this first virus, this is a typical human seasonal epidemic virus, H1N1pdm09 virus. We have positivity for InfA, pdmInfA and pdmH1. And some of the other viruses that we have, we may have a delay in the week, or a week positive in the pdmH1 target as you see in the Ohio/24 virus, or actually, not see that target light up at all. pdmH1 is not necessarily indicative of all H1N1 B viruses, or H1v viruses that we may see.

In H3N2 viruses, we generally have an InfA positive and a H3 positive. And then we typically see that H3 being positive and all of the cases that we have of H3N2v viruses, or H3v viruses. Those, but also have that additional pdmInfA target as being positive as well. So be on the lookout for those. And those viruses that test in this particular manner can be called a presumptive H3b at the state. But we would like to see them at CDC to test them further and characterize them further. Next slide, please.

We do have quite an outbreak of H5 right now in birds, backyard flocks, and also poultry farms. And so there is a guidance for information for people exposed to birds infected with avian influenza we have on the flu website. Please check that out. We also have our CDC human influenza virus real-time RT-PCR diagnostic test for those that you can be used for screening those.

Please be aware that any positive PCR for H5 would be considered select agent, and must be reported as such immediately and shipped to CDC per select agent guidelines. So please be aware with that. In conversations that we've had with the Division of Agricultural Select Agents and Toxins, this is their interpretation of that, and we want to make sure that all labs are adhering to this until we have further guidance. If you have cases in which you have people that have been associated with culling birds on affected forms, the other option is to just to test them with your A/B typing, A subtyping. And then if you have a non-subtyped virus, then you can send that to CDC for us in order to get it into CDC's hands more quickly, particularly from those personnel. Next slide, please.

H5 guidance continuing, so anything that we have as a presumptive positive, which would be both targets, H5a and H5b are both positive, or an inconclusive result in which H5, one of the two targets is positive, we really want to see at CDC if any positive PCR for H5 be considered a select agent. It must be reported, and handled, and shipped per those guidelines as such. Next slide.

For H7, very much the same guidance. The specimen is only “influenza A detected and subtype Eurasian H7 detected” if both targets, InfA and EuH7 are positive. If it is not positive for the InfA target, and only positive for the H7, then it would be inconclusive. Positive PCR for H5 and H7 would be considered a select agent again, and must be shipped per guidelines. And next slide.

So here's the shipping information. Please ship these to CDC to me. Influenza A that cannot be subtyped, any presumptive positive of H3v, or any zoonotic viruses, H7, H5 viruses can be shipped to me as well. Send these clinical specimens for further characterization to my contact, and here it is. And please note that anything with a greater-- that cannot be subtyped with an influenza A CT of greater than 35 may be reported as inconclusive. Our subtyping primers are often don't have the same LOD as our typing primers. And that is partially by design. And so if they are greater than 35 CT, then they are really, really close to the LOD of the assay, and probably are intermittent in their positivity, or may not work at all. And with that, I'll close, Sean, and take any questions.

SEAN COURTNEY: All right. Thank you for that, John. Really appreciate that update today. A couple of quick questions in the Q&A. The first is, is it recommended to test for both COVID and influenza PCR for symptomatic patients?

JOHN BARNES: Yes, we would like to, because right now, when we deal with-- even if you're going to ship it into CDC from one or the other, it is helpful for us to understand if it is a COVID positive or influenza positive. CDC is still handling COVID positive samples for clinical specimens and BSL-2, plus and for grown specimens in BSL-3. And so it helps us understand where those need to be handled.

SEAN COURTNEY: All right. Thank you. Next question was, how do you test for H1pdm09 or the H3 types?

JOHN BARNES: So the CDC has assays that they've developed and shared with our public health partners, and which does have targets for both of those types. They target the HA of both of those types. And we do that with real-time PCR. If you're interested in getting those tests, or available to get those tests, and you can either work with their public health lab in your area, or you can reach out through IRR and see if you're eligible to receive those kits.

SEAN COURTNEY: Great. Thank you. Next question that just came in was, can the BioFire Torch pick up these rare subtypes of flu?

JOHN BARNES: So we did run some very rudimentary assays on the BioFire to see if they would actually detect the new H5N1 as circulating around in birds, and it will. I'm not a 100% confident on the limited detection. I did not have the capability of doing that to see if it is fully maintained a limited detection it usually has or not. But it will pick those up to our knowledge.

SEAN COURTNEY: Great, great. Thank you. And I do not see any additional questions at this time. So I'm just going to go ahead and say thank you for that, and really appreciate you joining us today on our call. And I would also like to go ahead and just thank all of our speakers today for joining us and having all these different discussions. I think they were really great to see all these different talks today. So that was really good.

And just as a reminder, we have our December call coming up on December 19. And that is scheduled at 3:00 PM on December 19. And again, just want to really thank everybody for joining us today. I know it's a holiday week for a lot of us. So hopefully, you all can get some time off and enjoy some time with families, and just really take some well-earned break. So with that, I'm going to end today's call, and thanks again for everybody for joining in. Have a good one.