Clinical Laboratory COVID-19 Response Call

November 16, 2020

Agenda

- **Welcome**
  - Jasmine Chaitram, CDC Division of Laboratory Systems (DLS)
- **ASM's Clinical Microbiology Supply Shortage Collection (CMSSC) Tool: Identifying Lab Supply Shortages in Real Time**
  - Melissa Miller, American Society for Microbiology (ASM)
- **Evaluating the Sofia SARS Antigen FIA for Asymptomatic and Symptomatic SARS-CoV-2 Testing on Two University Campuses – Wisconsin, Sep 29 – Oct 9, 2020**
  - Ian Pray, Wisconsin Department of Health Services
- **FDA Update**
  - Tim Stenzel, U.S. Food and Drug Administration (FDA)

JASMINE CHAITRAM: Hello, everyone and thank you for joining the Clinical Laboratory COVID-19 Response Call. I am Jasmine Chaitram, I am the Associate Director for Laboratory Preparedness inthe Division of Laboratory Systems at CDC. The Division of Laboratory Systems, or DLS, has been hosting these calls since March and we hope you find them useful.

The Division of Laboratory Systems at CDC has been working with public health and clinical laboratories before the COVID response on various topics including biosafety, data science, biorepository science, informatics, workforce competency, and training. We've also worked on preparedness and response issues. And since the COVID pandemic we have been working with the CDC Emergency Operations Center serving as a liaison between clinical laboratories and public health laboratories and CDC. We've been hosting these calls to provide hopefully relevant and timely information to all of you.

I'm showing today's agenda. We've got two great speakers lined up for you, as well as Tim Stenzel from the U.S. Food and Drug Administration as our regular agenda participant. And before we get started I'm going to do a couple of housekeeping things.

So first up is that we have our calls on Mondays, every other Monday, and our next call will be on November 30 from 3:00 to 4:00 PM. Look forward to having you join us on that day. We want to hear feedback from you, especially on training and workforce development issues. So please email us at LabTrainingNeeds@CDC.gov.

We also provide resources in the slides, links, information. The slides are available after the call, usually within a week, as well as the transcript and the audio from the call. So you can download those if you need to, and they're on the DLS web page, Preparedness. I think I have a slide showing you the web page, but the slides are there as well as all of our-- here it is as I was

talking about it. Here is our Preparedness Portal, so you can go to this link and find all the information from our previous calls, as well as LOCS messages and other COVID-related information.

We also recently posted updated point-of-care testing information on our webpage. Please visit that page, it was recently updated with some frequently asked questions. And then finally, how to ask a question, please use the Q&A button in the Zoom webinar system to type your question. As a reminder, it would be helpful if you include your email address. We do try to answer all of the questions on the email but sometimes they're not able to because of the number of questions coming through. And so if you provide your email we can follow up and provide a response at a later date.

We do apologize in advance if your question is not answered on the call. As I mentioned, we do our best. Please, also submit any ideas that you have or specific wants or needs as far as agenda items for future calls. We do review all the information in the Q&A box and it does help us with future planning.

And with that, I think I'm going to go ahead and move to our first speaker, who is going to be Melissa Miller from the American Society for Microbiology. And she's going to be talking about a survey that was recently hosted by ASM. Melissa?

MELISSA MILLER: Great, thank you for having me. I am Clinical Microbiology Director at UNC Chapel Hill, but what I'm presenting today is with my ASM hat on. I am the chair of the Clinical and Public Health Microbiology Committee. But there are many people within ASM that worked on getting this tool together because we were hearing from our members, mostly clinical and public health microbiology members, that they were dealing with a wide variety of shortages.

And I'm sure many of you on the call can recognize that we're all dealing with this. So what's the scope of what we're dealing with, and by gathering information can we transparently make this available and then potentially get some action to fill these challenges. So next slide, please.

So our position is by tracking these supply shortages this will allow us to make data-driven decisions and work with our federal partners, perhaps, to get some relief in some of these decisions in terms of allocation and even just knowing where the shortages are. So ASM, in partnership with the Association of Supply Chain Management, if you didn't know that existed now you do. And they're really amazing experts in terms of supply chain as a whole.

So they work together on an online platform to track supply shortages and clinical labs. So we began collecting data from CLIA-certified laboratories on September 11th. And it's a weekly survey, and labs can submit the survey information as they get to it throughout the week. It's open and you just put in the date that you are entering the data for and the supplies you have at that time that you're submitting the survey.

The survey was issued to 300 of our national network of laboratories, so these are high complexity laboratories that these were targeted to. So we monitor both COVID-19 and non-COVID testing supplies. The non-COVID testing supplies, you know we were all focused on COVID testing and supply chain early on, and now this has switched back as all of our institutions have opened back up. And now we're also dealing with non-COVID testing supply shortages.

We want to be able to identify these in real time. And obviously lack of supplies really impacts our day to day laboratory operations. Next slide, please.

So this, the data are updated every Tuesday with the survey data from the week before. So the numbers I'll be presenting today are those that were uploaded to the website as of last Tuesday. You can check, there's a link at the end, you can see the updated data should be updated tomorrow. So many of our labs can't perform routine tests or we have limited availability to do some tests. So about 47% of labs reported shortages of testing supplies for routine bacteria.

So this is mostly culture-based media that were on shortage. Sometimes we had to switch gears and use maybe a piece of media that wasn't as good for what we intended, or maybe even a different manufacturer of media. And some of these come with challenges that we have to validate them and do additional quality control when we get these into our laboratories.

57% reported shortages of supplies for the molecular detection of sexually transmitted infections. And I'll show you the longitudinal data of these in just a minute. But this is really, I think, what's striking to me. And I think the highest that was reported was the first week of the survey, which was about 89% had shortages.

And I know even in my lab we had to stop testing males for chlamydia, gonorrhea, and trichomonas because we didn't have certain supplies. 15% have shortages for mycobacteria testing, and about half face shortages for routine fungal testing. Next slide.

So ASM has been actively involved throughout the pandemic in terms of addressing supply shortages. We've provided input on FDA regulations, in EUA and worked directly with the FDA early in the pandemic to really allow CLIA-certified labs to use their own tests to get those tests out quickly. ASM was among the first to sound the alarm, looking as early as March, asking for increased funding to address shortages. ASM issued a letter to the White House Task Force urging transparency of resource allocation. So this has been a problem throughout the pandemic.

In terms of data collection, as to my knowledge, this is the most robust online platform to monitor and report laboratory shortages. And again this is being done in real time. And lastly calling on Congress to provide continued relief for COVID-19 and advocated for emergency supplemental appropriations and renewal of the PHE, Public Health Emergency Declaration. Next slide.

So now we'll get into some of the details of the survey and what it's showing us. So this slide not only shows you the laboratories who have been reporting, but these are the COVID-19 based test data. So these are RNA-based tests that we're talking about. So labs on average said without resource constraints they could do just under 1,700 COVID-19 PCR-based tests in their laboratory. On average over the past seven days they had been doing about 800 tests.

So this is indicating that we're at about 47% testing capacity utilization. So in theory we can do a lot more testing than we're currently doing. And as you see all the spikes and the increased need for testing coming towards us this will be really important to make sure we're doing testing at our greatest capacity. Next slide, please.

And this is just tracking those data test utilization over time. So as it has gotten better over time you can see the scale on the y-axis is really between the 35% to 50%. We're still remaining in that range. Next slide, please.

So in terms of just showing the data, in terms of the gap between in red the capacity if we had no constraints, you can see that the capacity just change a bit from week to week. This does maybe have to do with particular details of certain laboratories, but it also has to do with who has reported for that week. So we will see some fluctuations week to week, but that gap has remained constant throughout the seven weeks of doing the survey. Next slide.

Here are the components breaking down to where the shortages are and color coded as shown to you along the x-axis again week by week. So that you can see the highest item in gray are other consumables. This is largely plastics, tips, even plate sealers. This is for laboratory developed testing, COVID-19 testing.

Master mix and reagents shown in green, instruments for nucleic acid extraction shown in yellow. So some smaller shortages, but still consistent shortages over week to week, with primarily focusing on consumables and then in red the extraction kits and consumables for extraction.

Interestingly, over the seven weeks we have seen an increase in shortage of primers and probes. I knew in our experience this is just a delayed time to being able to get them because of slowing manufacturing. Next slide, please.

So in terms of commercial COVID-19 PCR tests you can see kits and consumable shortages remain very high throughout all of the weeks. Maybe steadily but slowly decreasing over the seven weeks. Instruments are still hard to come by so those of us who might be trying to increase capacity beyond what we have, either to make up for supply shortages or to get ready for the surges as they come along, these currently are still about 30% of laboratories have shortages of trying to get instruments.

Control materials vary from week to week. Actually we've had no back orders of control materials in 10-- actually, I just got an email about 30 minutes ago that we have two days of control materials left. So it's a day at a time for many labs. Next slide, please.

So in terms of non-COVID testing supplies, this was perhaps a bit of surprise for some of us when all of our institutions started opening back up and more procedures being done and we got busier. Then all of a sudden we weren't able to get all the supplies as we used to be able to get. So again, the number of labs reporting shortages you can see the highest are for bacteria. Again this was largely culture media. And then in the teal color STI testing.

But fungal, honestly, has been pretty consistent throughout the seven weeks as well. Either media or even some of the stains to look directly at specimens have been in short supply. Whereas mycobacteria and parasitology has had some reported shortages, but not to the extent of the other areas of our laboratories. Next slide, please.

These are the number of days surveyors are asked to estimate the number of days testing remaining. And again, this is going to be a very dynamic number depending on the volumes of specimens that we're getting. But you can see it's anywhere from just a few days to maybe about 20 days at the most for some of these supplies. And while this may sound like a lot, I mean, I think the challenge is not knowing when your next shipment is coming.

So many of the media that we have that are back ordered for example, have release dates of July 2021. And so we're really forced to look at additional media types and other types of consumables that we're not able to get, which is not always a one to one swap. Next slide, please.

You can access these data at the link shown here. You can also, if you just Google ASM supply shortage it's the first thing that comes up. And the updated data will be available on the website tomorrow. Next slide, that might be the last slide. So if you have questions, you can email clinmicro@ASM.usa.org, or contact them at the phone number listed on the slide. Thank you so much.

JASMINE CHAITRAM: Thank you, Melissa, it was a great presentation. We do have a couple of questions for you right now. The first one is, are there plans to expand the survey base? Are you going to add more laboratories to the survey?

MELISSA MILLER: That's a good question. I'm not exactly sure how wide the survey will be distributed. The link is active, actually, so it doesn't restrict people from responding to this survey. But I can get clarification from ASM and provide information back to CDC about how widely this can be extended.

We do collect CLIA numbers of laboratories so we can make sure, even though the information doesn't go anywhere, it's all private and it doesn't go anywhere outside of ASM, we do collect

the CLIA numbers so we can tell who is responding to the survey. So I will get clarification on that.

JASMINE CHAITRAM: OK, that would be great. The next question says, Can you comment on the success of your efforts to get more of the necessary supplies identified in your study? I don't know if ASM has been doing anything in particular.

MELISSA MILLER: Yes, so certainly we've had conversations with federal partners. This has gotten a lot of attention on that scale. Also in the media, I've talked to three different people today who are keenly aware of the shortages. So getting the word out is really the first step. Hear us, we've been screaming that this is an issue. And so we really need to make sure that we can get to the people that have some sort of input over the supply chain.

You know, ASM or me, myself can't fix the supply chain, right. But it's trying to get to those partners that can help this. So I do think that the idea is primarily to get the data out, to make sure it's transparent what's going on with these, and engage with our federal partners.

In terms of has the survey directly had an impact on supply chain, I would say not yet because we're at the early stages. And we needed the data first to indicate to us how extensive and was this a consistent problem. We didn't know if it was two or three weeks and then it would be better. But now we can see it's a consistent problem. So hopefully can get action soon.

I did get a clarification from ASM that any lab can participate in the survey.

JASMINE CHAITRAM: Wonderful. It's just another comment in the Q&A box is that the labs have seen the survey once. Are you circulating it weekly? Can you explain a little bit about the link and if it's just always there and available?

MELISSA MILLER: The link is always there and available. So actually what I did is I made a calendar Outlook invite on my calendar every Wednesday. And I put the link there so I would remember every Wednesday to go in and report our shortages. Keep in mind, if you don't have shortages we need to know that, too. So just always fill out the survey because we need to understand both when you have shortages and when you don't.

The link is, and reminders for the survey do go out weekly, but again the catchment area that maybe the person was typing from may not be getting it weekly. I'm not sure. But I know the initial community of 300 labs that were invited to do the survey does get a reminder sometimes more than once a week. Because there are weeks that we have lower participation. Again, it is a challenging and busy time for everyone. So we appreciate anyone who can do the survey.

JASMINE CHAITRAM: OK great and then somebody asked about sharing the link again. And I'll just comment that the slides will be available on the Preparedness Portal so you can check the slides if you need to get access to the link. OK. I think there's one more question for you,

Melissa. Do you think in the long perspective will the Defense Production Act be helpful in production of supplies?

MELISSA MILLER: I don't have the expertise to comment on that. I can't predict whether that will be helpful or not. I'm hopeful that it would be, but I'm not the right person to contact on-- to comment on that. Sorry.

JASMINE CHAITRAM: OK, well thank you very much for joining our call this afternoon. I appreciate the presentation and answering all of the questions.

Our next speaker today is going to be Ian Pray from the Wisconsin Department of Health Services. And he's going to be talking about initial results from CDC antigen test study. Ian? I think you're on mute.

IAN PRAY: There we go. Can you hear me?

JASMINE CHAITRAM: Yeah.

IAN PRAY: Not yet, now you can. OK, great thank you. All right give me just one second here. OK, great. Thanks for having me. So yes my name is Ian Pray. I am an epidemiologist, and Epidemic Intelligence Service Officer with CDC appointed to the Wisconsin Department of Health Services as a field officer.

So today I'll be sharing preliminary results from our evaluation of the Sofia SARS Sofia Rapid Antigen Test, which we did at two universities in Wisconsin in September and October of this fall. So this test is, I'm sure you're all familiar with it, this is known as the Quidel Sofia rapid antigen test or a point-of-care test. It's one of the more popular point-of-care antigen tests that's received the emergency use authorization. Next slide.

I don't have to tell you all that there are a number of potential benefits of rapid antigen tests. They've gained quite a bit of popularity and grown in use over the last few months. Obviously they can be used at the point of care, they're low cost, they allow for rapid return of results. And for those reasons they've become quite popular and quite widespread use now in a number of settings. All of the available antigen tests, rapid antigen tests, are authorized for use on symptomatic patients within five to seven days of symptom onset currently.

For the Sofia Rapid Antigen Test, it's symptomatic individuals within five days of their onset date. And initial data that was submitted to the FDA for emergency use authorization for all of these platforms, including the Sofia, were quite promising. For the Sofia, we've reported there was a 97% or 96.7% I think sensitivity and 100% specificity. But that is again, used within the predetermined population, symptomatic individuals within five days of symptom onset.

So we all know that in many settings, rapid antigen tests are being used off label. So this would be widespread use in asymptomatic populations, college campuses, nursing homes,

workplaces, correctional facilities, other settings. And there's is a significant lack of data evaluating their accuracy in these populations. And there's a number of CDC supported field studies that are underway right now to evaluate these different test platforms in a number of different settings.

This is one of them, one of the earlier ones that was done and we now have data on it. We're happy to be able to share. So in mid-September the Epi studies field team deployed a team to Wisconsin with the objective of evaluating the diagnostic performance-- oh, excuse me, next slide, please. There you go.

The objective of evaluating the diagnostic performance of the Quidel Sofia SARS Antigen FIA, compared to RT-PCR and viral culture in asymptomatic and symptomatic persons at two universities experiencing increased COVID-19 activity in September. Next slide.

And just a little bit of background of Wisconsin. As you all know, and similar to many other parts of the country right now, Wisconsin is currently experiencing a surge in COVID-19 activity, new daily cases on a steep upward trajectory that started around the beginning of September here in Wisconsin. The current increase began in late August, early September, roughly correlated with a return to campus for a number of large universities in the state. And the graph on the right there shows increased activity among 18 to 24-year-olds, which does correlate in time with return to campus for the fall. Next slide.

So the way we set up the study is we did, it was at two different campuses, and we did sample collection on these two university campuses. We embedded the study in their routine testing protocols that were already going on on campus. This included at one of the universities testing of quarantined students who had a known exposure to COVID-19 and were in quarantine housing at the time of the test. And at the other university it was during their weekly surveillance testing, this was mandatory testing for all on-campus students, and optional testing for other students and staff.

So the investigation participants completed a questionnaire. We then took two mid-turbinate swabs, simultaneously collected one in each nostril and then swapped for the other nostril. And one of those swabs went for Sofia Rapid Antigen Testing and the other went for RT-PCR testing. Overall between the two campuses we collected 1,098 paired specimens from a variety of students, staff, and other university affiliate. Next slide.

Looking at the population of people that were tested, of those 1,098 paired swabs that were collected 41% were from males, 90% from students, 70% were from students living on campus and residence halls. And then for regarding symptoms there were 79% of the population was asymptomatic at the time of specimen collection. With 21% having at least one symptom that they reported on their questionnaire at the time of testing, and 14% when we looked closer at the symptoms met the CSTE clinical criteria for COVID-19 with two or more symptoms. Or it's a little bit more complicated than that, but one of a few symptoms and then two or more of a few other symptoms. Next slide.

So this plot is showing the initial prevalence in the different groups as measured by the antigen test in the blue bars and the PCR testing in the green bars. So overall we had about a 5% prevalence rate among the participants by PCR, 2% among asymptomatic individuals. And then looking at people with symptoms, 18% prevalence by PCR among people with at least one symptom. And then with more symptoms meeting the CSTE clinical criteria, 24% prevalence. That's on PCR.

And then for the antigen test prevalence was 5% overall with a slightly higher prevalence among asymptomatic individuals due to some false positivity, which we'll get into. And a slightly lower prevalence for symptomatic individuals compared to PCR due to some false negativity which we're going to talk about in the next slide I believe. Go ahead.

OK so this has a lot of data on it, but I'll try to walk you through some of the findings here. So the comparison of antigen test results to RT-PCR is shown here, stratified by the presence of symptoms at the time of testing. So beginning with symptomatic persons on the left side of the plot, test sensitivity was 80%. That included results-- positive results from 32 out of 40 of the PCR positive participants having a positive rapid antigen test. And specificity with 98.9% in the symptomatic group. So there were a total of two false positives and eight false negatives, which led to a reasonably high positive and negative predictive value of 94.1% and 95.9% in the symptomatic group.

Moving over to the asymptomatic persons on the right. Test sensitivity in this group was quite a bit lower, 41.2% among asymptomatic individuals. That came from 7 out of 17 PCR positive asymptomatic individuals receiving a positive antigen test. Specificity was 98.4% and looking at, we had a total of 14 false positive results in the asymptomatic group and 10 false negative results in that group. So with a lower prevalence in this asymptomatic group and the lower specificity and the lower sensitivity, positive predictive value was down to 33% in this group for the positive antigen test. Negative predictive value with 98.4. Next slide.

So now here we've plotted out the different sensitivity, specificity, positive predictive value, and negative predictive value by a variety of groupings based on the population. At the top of each graph we see the values among participants who showed any symptoms at the time of testing, and then people who met the CSTE clinical criteria. And then next participants with any symptoms within the five days of symptom onset, and then finally, people that were currently asymptomatic. Followed by people who were asymptomatic for the full 14 day period. So you can see that the sensitivity was a bit lower as we went through those different groups. Next slide.

OK, so taking a look at the viral culture results, which think is an interesting component of this study. So we ended up sending 73 specimens for viral culture representing those that were positive by antigen test or by PCR tests. So everything that got a positive on either platform was sent for culture. We got a total of 34 positives by culture. This included-- sort of breaking this down by category-- this included 32 of 39 of the concordant positives, so antigen and PCR

positive. 2 of 8 false negatives, from symptomatic participants, 0 of 10 false negatives from asymptomatic participants, and 0 of 16 of the false positive results.

So this tells us that 16 of the 18 results that were negative on antigen but positive on PCR were not positive on culture. The flip of that is that there were two culture positive individuals that received negative antigens tests. Importantly, both of those individuals we re-swabbed two and four days later and were positive on both antigen and PCR tests.

So the graph on the right shows the same, this viral culture and antigen data, but now broken out by days since symptom onset and the N1 Ct values on the PCR. So of the 57 PCR positive samples that are included here, the samples that were positive on viral culture, which is the red on the graph, had significantly lower Ct values, indicating more viral RNA. Compared to samples that tested negative on viral culture. And none of the PCR tests with Cts above 30 were culturable.

Similarly samples that tested positive on the antigen test-- so those are the Xs on the graph-- had significantly lower Ct values and were more likely to be cultured compared to negative antigen tests. OK, next slide.

All right, so kind of trying to summarize our findings here, we can say that when we used these rapid antigen tests, the Sofia Test specifically, for diagnosis and individuals currently experiencing COVID-19 symptoms, the Sofia Test had lower sensitivity and a lower specificity than reported in the FDA EUA data. The decline in performance was particularly true among asymptomatic individuals, where sensitivity was 41%. And because of some false positive results and a lower prevalence in the asymptomatic group, the positive predictive value was low at 33%. And then the results of the viral culture told us that while positive antigen results did correlate well with the ability to culture the virus, there were those two specimens that were culture positive and tested negative on the rapid test.

Kind of stepping back and thinking about how this might influence how we think about testing, testing protocols, and follow-up testing using the antigen test, based on these results, at least within this study, our conclusion was that testing strategies should certainly consider confirmatory molecular testing. If there's a negative antigen test in a symptomatic individual, so if COVID-19 is suspected, and that because of the somewhat lower sensitivity in this group, follow-up PCR test if a negative antigen test is received would be advisable. And then on the flip side of that, a positive antigen result in somebody who's asymptomatic and/or the pre-test probability is low, to consider receiving a confirmatory molecular test in that situation as well.

I anticipate that these-- anyway, that's the end of the formal presentation. I can take questions. This is in review right now, hoping to be published as a MMWR report in the next few weeks. And still going through clearance, so I'm sure that we'll have continued discussions about how to apply this data and how that might influence any kind of testing protocols, which has not sort of been incorporated into current guidance. And that's all I have, thank you.

JASMINE CHAITRAM: Thank you, Ian, very much. That was a great presentation. We do have some questions. The first one is what was the real time PCR platform that was used in the study?

IAN PRAY: So they were two, so it depended on the university. The vast majority of the samples were run at the PCR-- excuse me, at the CDC's surge laboratory, by CDC Surge Laboratory Group, and used the CDC PCR. The PCR test that has been developed by the CDC's laboratory group. I'm not sure if I can go more specific than that. I could look up the actual name. I think it's called CDC COVID-19 PCR, something like that. Somebody from the Division of Laboratory Systems can probably answer that better than me.

And Then there are about 50 of them were run at the University of Wisconsin's Veterinary Diagnostic Lab and they were using-- what was it, I'd have to look it up in the manuscript report. Because I don't have it on the top of my head. I'll put it in the chat in a minute.

JASMINE CHAITRAM: OK great, that'll be fine. OK, the next question is, do you have any assessments of the causes of false positives? Were they operator error, cross-contamination, instrument overheating, anything like that?

IAN PRAY: Yeah it's an interesting question. And we certainly looked very closely at those false positive results. And I could share an anecdote. It didn't really tell us what-- so the short answer is, no. We weren't able to identify any clear cause of the false positive results. But sort of the interesting nugget was that eight-- so we had a total of 16 false positives in our whole group. Or 18, 16, excuse me. 16 false positives in the whole group.

So eight of those happened within a very short amount of time at one of the testing sites. Nearly sequentially, there may have been a few negatives interspersed. On the same machine, same lot of tests, and with the same technician running the samples. So we certainly looked very closely at those. We didn't identify any user error or breach of the instructions for use or protocols. It seemed that the technician was doing everything according to plan.

We did, because that was flagged pretty immediately that there was a unusual spike in sequential positives on the antigen test, we were able to bring six of those individuals back and re-swab them within an hour. And those were all negative. So we were pretty sure that this was not a they were obviously not-- and they were also negative on PCR obviously. So something happened, we didn't find an ultimate cause for it though.

JASMINE CHAITRAM: OK one other question, did you try nasopharyngeal swabs?

IAN PRAY: No, we did all mid-turbinate swabs. So the majority of them were collected by medical personnel. We weren't trying-- we weren't testing or evaluating swab types or practice protocols.

JASMINE CHAITRAM: OK, all right, well thank you very much. In the interest of time, I'm going to stop there with the questions, but they are in the Q&A box. So if you wanted to look through them and answer some in the chat you can do that. And I think folks would appreciate if you provided information about the PCR platform. And thank you again for joining us this afternoon.

IAN PRAY: I'll put that in right now.

JASMINE CHAITRAM: Yeah, thank you again for joining us this afternoon. Before we get to our last speaker I did want to mention a couple of things. First, we are getting a bunch of questions about the IQCP. And I know that we recently sent out a LOCS message, that's the Laboratory Outreach Communication System email that we send out to clinical laboratories. And we recently sent a message about this from CMS. And we don't have anybody from CMS on the call today. So what we are going to try to do is have somebody from CMS participate in the next call to answer these IQCP questions.

And what we'll do is send these questions in advance to the speaker so they can prepare to answer them on the next call. So appreciate your patience with that. I also, we have a couple of biosafety questions that have come through and we do have somebody from biosafety on the line. Aufra Araujo. OK, I've practiced it, but I of course couldn't say it live perfectly. But anyway, Aufra is from the Division of Laboratory Systems and she is our biosafety SME right now. And I'm going to ask her if she could answer a couple of those questions for us. Hang on, Aufra, are you there?

AUFRA ARAUJO: I'm here. Can you hear me, Jasmine?

JASMINE CHAITRAM: Yes, I can. OK, so a couple of questions for you. How should tests-- and this is a new question that we got in just now-- how should used test cards and test wrappers for the swab be disposed of after the facilities perform point-of-care testing?

AUFRA ARAUJO: So both used test cards and the test wrappers for the swabs, if the test wrappers, if they are potentially contaminated they should be discarded as biohazard waste. So handle laboratory waste from testing suspected or confirmed COVID-19 patient specimens as all other biohazardous waste. Additionally, it seems waste regulations vary from state to state. Disposal must comply with all local, regional, national, and federal regulations. So personnel should follow guidance in accordance to federal, state, and local regulatory requirements. And laboratories should also perform a site-specific and activity-specific risk assessment to identify and mitigate risks.

JASMINE CHAITRAM: Thank you, Aufra. And I've got another one for you. Is it safe to send COVID-19 dry swabs placed in plastic screwtop tubes through the pneumatic tube system?

AUFRA ARAUJO: No, so CDC recommends to **not** transport COVID-19 respiratory specimens through pneumatic tube systems or PTS. The current guidance provided by CDC recommends

that respiratory specimens from patients with suspected or confirmed COVID-19 should **not** be transported through the pneumatic tube system. And--

JASMINE CHAITRAM: Great, thank you. Oh, go ahead, keep going.

AUFRA ARAUJO: I was going to say at this time this recommendation only applies to suspected or confirmed COVID-19 respiratory specimens. And some examples of these respiratory specimens include nasopharyngeal and oropharyngeal swabs. Nasal, mid-turbinate, and bronchoalveolar lavage, sputum specimens like that. I also can add that this is a recommendation based on currently available data. Other types of specimens such as blood, urine, and feces are still acceptable to transport through pneumatic tubes. And like anything else in the lab, facilities should ensure that all personnel who transport specimens via the pneumatic tubes are trained in safe handling practices, specimen management, and skilled decontamination procedures.

JASMINE CHAITRAM: OK, thank you very much. And that's it for the biosafety questions. I appreciate you jumping on the call to answer those today.

OK, our last speaker for today is Tim Stenzel from the US Food and Drug Administration giving the FDA update. And just a reminder, there are just a couple of background slides with FDA links and email addresses and important phone numbers. But other than that, there aren't any other slides. And Tim, are you ready?

TIM STENZEL: I am, thank you, Jasmine. We have a number of questions Hopefully I can get through them in the time remaining. So there's a question about is there any update on the BD MAX SARS-CoV-2 Reagents? Currently, there is a limitation presumed negative-- or presumed positive rather limitation. And no, there isn't an update at this time.

As soon as we authorize an update we will post that very quickly after that FDA authorization is made. And so I would direct further questions to BD if you so choose. But obviously we actively work with any developer and try to authorize any updates such as this as quickly as possible.

The next question is, is there anything in literature about collection variation on the same patient? So I'm not exactly sure where this question is really going. I'm assuming differences between sample types, so interior nasal, mid-turbinate, NP, perhaps saliva. And there is variation reported in the literature and in the data that we have reviewed. So I'm not exactly sure where that's coming from, but-- so it is because of the various shortages, because of the risk to provider health by doing an NP swab, for example, we aren't requiring NP swabs where they might be the most sensitive. And we're open to the different sample types once validated.

So the next question is can self-collected nasal mid-turbinate be used for influenza testing? So I think the emphasis here on self-collected. There currently no flu tests have been authorized for self-collection. We did issue a recent guidance titled Enforcement Policy for Modifications to

FDA Cleared Molecular Influenza and RSV Test During the Coronavirus Disease Public Health Emergency.

And this does include a policy regarding modified a cleared test to add health care provided collected interior nares and mid-turbinate specimens. But it specifically excludes an indication for use that involves self-collection. So in particular any kits that want to have a self-collection or a home collection situation does require an authorization. Though we're open to reviewing data and making authorizations as supported by data.

Next question is, a recently released EUA molecular test states that a negative finding is to be considered a presumptive negative result. If this testing is used following a negative antigen test results to provide a confirming molecular test, is an additional molecular test required if a negative finding is revealed by the first molecular test? So what I take this as is that you have two negatives. Do you have any requirement to do anything else? And no, in fact there is not a requirement to reflex the negative, the first negative on the antigen. It's just if there are any clinical concerns about that patient then use good clinical judgment to determine whether a reflex to another molecular test.

So the next question is for FDA, what are authorized collection devices for blood in stool? There are authorized collection devices for blood in stool but not for COVID, which I presume that's what the question is about, as far as diagnostic assays. Of course, for serology blood is the expected sample type, either whole blood, plasma, or serum. And those collection devices are authorized for general use, usually in blood. Blood cards are a different thing for serology, though. I don't believe we've authorized a blood card for serology especially for COVID yet.

So again, not sure of the exact nature of this question. So if any questions I'm not addressing appropriately you can email. And it's posted on the presentation here, I believe. You can email the FDA at-- thank you, Jasmine, CDRH-EUA-Templates@fda.hhs.gov.

Next question, if an FDA EUA assay is approved for pooling does an individual lab need to submit an FDA submission? No not for use with that authorized kit at all. And in fact, we're not requiring modifications of kits by labs to be submitted. But if you want to use an EUA approved method we recommend using obviously a kit that's authorized for that and to follow those kit instructions. We worked closely with those developers so that there wouldn't be a requirement for individual lab validations of the pooling. The way we authorized it, if you follow the instructions they do recommend taking a look at your-- I believe usually your historical information. So do follow those instructions as a recommendation for using pooling with those kits.

What about using the pooling for asymptomatic individuals? So if it's an LDT we're not asking for submissions right now. And I do recommend that even if there isn't a claim for asymptomatic individuals but if you get a valid order that you do perform that testing and report it out. And as we've seen in the prior presentation, performance on asymptomatic

patients can obviously vary. That's not surprising data to anyone at the FDA who's reviewed a lot of applications in the asymptomatic population.

So again, clinical judgment is important in this and knowing if a negative result should be followed up with perhaps another type of test. Or perhaps a single test rather than a pooled test. And kits that want to make claims for either asymptomatic or pooling, we do want to require an EUA authorization.

Last question in this part is how is pooled testing reimbursed. This is not an FDA question. So I would refer you to CMS and/or the insurance companies that your lab sees.

Next question, is an EUA still required when implementing pooling on an LDT for molecular COVID-19 testing? No, not for pooling. There is the caveat that if you are doing home collection self-collection offsite, that we do ask for any EUA submission for that situation. But typically that's not how pooling is done.

And I believe this is the last question. Our organization is experiencing an urgent request from a state to expand COVID-19 testing. The only way for our organization can meet this request for expanded testing is to test saliva specimens that have unobserved collections. We would like to support our state but are committed to remain in compliance with regulations and standards. We would like to know the regulatory stance on testing saliva specimens with unobserved collection.

So we are not asking for submissions if the unobserved collections are happening within a health care facility, including any temporary facilities for which the collection may be unobserved. Except for maybe the exceedingly rare situation where an authorization that we've made, the letter of authorization and the IFU for that test specifically does not allow self-collection. So it would be worded very clearly. And if there is one, there's only like a few that I even think are relevant. But I always like to say that because I don't like to make a blanket judgment if we've reviewed data and haven't been able to support say self-collection.

There are two authorized saliva collection devices if you want to use them that can be used to collect saliva unobserved at health care sites. Look to our FDA authorization page for that. And then for home collection, please follow the home collection template for information on manufacturing and submitting an EUA request for a home collection kit. And so, that's the end of the questions I have prior to the call. Thanks, Jasmine.

JASMINE CHAITRAM: Thanks, Tim. Actually, I do have a question for you that came through today during while you were speaking. The question is, do you need to validate different VTM manufacturers and swabs separately on your platform if you need to switch to a different supplier?

TIM STENZEL: That is a great question. Tip manufacturers are used to these kinds of swaps, and if it falls within their quality system to do that there's really switching vendors is not an issue if

the formulations are basically the same as the ones you have been using. And for labs, we're not reviewing those kind of things. I think for a long time through our FAQs we haven't been reviewing those changes. And we'd just refer those labs to-- or we would recommend that they follow any sort of CLIA requirements for those switches.

JASMINE CHAITRAM: OK and now one more for you, Tim. Does the Flu A, Flu B, and SARS-CoV-2 laboratory developed test require an FDA EUA submission?

TIM STENZEL: If it's to be run by health care collected or self-collected on site samples on a health care facility and it's an LDT, developed, designed developed, manufactured, validated, in a single lab, no. No we don't-- we're not asking for submissions of those.

JASMINE CHAITRAM: OK, as always thank you, Tim, for joining these clinical lab calls. Appreciate you spending the time answering these questions.

TIM STENZEL: You're welcome.

JASMINE CHAITRAM: And that is our agenda for today. And I know that there were several questions, like I said, that came through that we were not able to answer today. But we will try to either answer them through email or on the next call. And as a reminder, as I had mentioned at the beginning, our next call is on Monday, November 30. We hope you can join us.

If you're not already receiving emails from CDC through LOCS please, sign up by going to LOCS@CDC.gov and sending us an email and telling us you're interested in receiving messages from us, and we'll put you on our distribution list. Thank you for all that you're doing out there. We hope that you're doing the right things, like getting rest as well, and staying safe. And thank you for joining us today on this call.