

Clinical Laboratory COVID-19 Response Call

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Panelists

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JASMINE CHAITRAM: Hey, everyone. I'm Jasmine Chaitram. Thank you for dialing into the Clinical Laboratory COVID-19 Response Call. I am with the Division of Laboratory Systems at CDC. And DLS has been hosting these calls since March 2020. And we thank you for joining us for these calls. The Division of Laboratory Systems has been working with clinical and public health laboratories. Traditionally, we work on biosafety, quality systems, informatics, biorepository, and data science, and workforce competency, as well as training.

We also work on preparedness activities and we have been serving in a role as a liaison between the clinical and public health laboratories and the CDC Emergency Operations Center during the COVID-19 response. We've been hosting these calls to provide information to all of you that might be of interest and to answer your questions. Right now, I'm showing the agenda for today's call. We've got some really interesting topics. I know that a lot of these things have been on your mind, so hopefully, we'll be able to answer your questions today.

And just real quickly, a couple of housekeeping things. Our next call is scheduled for Monday, August 17, from 3:00 to 4:00 PM. We are hosting these calls every other week now. And a reminder that the call information, the transcript, and the slides are posted on the CDC website-- it's <https://www.cdc.gov/safelabs/> under Tools and Resources. And so you can always go back there and here's the transcript again or see any of our slides. And we include a lot of important links on these slides, so it's a good resource for all of you.

One other quick thing I wanted to mention. A new slide that we've added this week is a list of programs that are offering proficiency testing for SARS-CoV-2. And a couple of things to just note. Six of the PT programs have modules for both molecular or antibody testing. The number of shipments and the number of samples in each of these PT programs vary. Several of the programs are working on developing PTs for antigen testing. And what I'm showing here is the website and contact information if you're interested. So again, I know these slides are going

pretty fast, but if you are interested and you want more information, visit our posting of these slides from today's call.

And this is our monthly survey that we're doing. Thank you to all of you that have participated in the past. Please continue to participate and give us your feedback. I do want to note that there are two questions on this month's survey about turnaround time, and we would like to get your feedback on that. It will help us in planning for our next call, which we'd like to focus a little bit about on challenges with improving turnaround time or some of the experiences that you're all having right now with delays in testing and getting those results out. So just please answer the survey, because it will help us as far as developing an agenda to address some of those issues.

And I've mentioned this before, as well-- the training and workforce development group at in our division of Laboratory Systems is wanting to hear more about your questions and needs around education and training. And for those, please send an email directly to LabTrainingNeeds@cdc.gov, as shown on this slide.

And then finally, the reminder about asking a question. To ask a question, please use the Q&A button in the Zoom webinar system. Type your question in the Q&A box and submit it. Be sure to include your email address. We do get a lot of anonymous questions, and it's difficult if we're not able to answer your question on the call to get that response back to you because we don't have your email. We will try to answer questions during the call. After our speakers talk, I will have a few minutes to answer questions.

But a lot of times, with the volume of questions that we're getting, we're not able to ask all of them, so we do try to get back after the calls and provide that information later. So thank you for submitting those questions. Have patience with us if we don't get through all of them during the call. We will try to answer them. And if, for some reason you don't hear an answer from us, you can always try to send your questions to us through DLSInquiries@cdc.gov.

And then two other reminders, if you're in the media, please contact media@cdc.gov. And if you're a patient, it's best if you direct your questions to your health care provider. And with, that I believe we're ready for our first topic, which is going to be an update on laboratory data reporting. And Sara Brenner, she has been on these calls before as a colleague from the Food and Drug Administration, but right now she's serving on a detail to HHS, the Department of Health and Human Services, and working on lab data reporting. And so Sara is going to give us an update on a few things. We sent out a [LOCS message](#) this past weekend with information and an implementation guide. And so more information from Sara. So thanks, Sara.

SARA BRENNER: Thanks so much, Jasmine. I don't have slides for today, but what I might do is drop a couple of direct links into the chat so that folks can go directly to the lab data reporting implementation specifications, which we're in short, calling the implementation guide. But as Jasmine mentioned, and thanks to her and many, many colleagues across HHS, and especially CDC, we were able to release on Friday afternoon just ahead of the August 1 implementation

deadline, the lab data reporting tech specs or technical specifications. I'll drop that link in as soon as I get done talking into the Zoom webinar chat, so you can go directly to it if you haven't already.

But essentially, I'll just give a couple broad comments about it, and then I'm happy to take questions later on if there's time. The intention of releasing this table, and it's essentially a field manual or a table, is as a complement to the June 4 guidance from HHS on COVID-19 lab data recording under CARES. And so essentially, what you see is a data element table from 1 to 30-some, and each data element that's listed in the guidance is in order there. What we tried to do is make it a little bit more readable and user-friendly in the sense that there are reporting requirements categories for federal CDC, HHS, state or local, and back to the ordering provider, with the intention of the data making it back into the patient's electronic health record.

We also provide a column of technical specifications that includes direct links to, for example, harmonized link codes for the test ordered and test results. And then in some cases, also, SNOMED CT values with direct hyperlinks. There's also a column with further examples listed and HL7 coding fields, again, with direct links, to those specifications.

So the intention of the table is to be used as a guide. For some laboratories, it's not nice to have, but they were already ahead of the game in terms of implementation. For other labs, we anticipate they'll really use it heavily, and it will really be a very helpful tool for them to have.

So a couple of other overarching comments about this guide or about the technical specification table. All of the data elements that are in here and listed as required were required in the June 4 guidance. So those that are listed as requested were also included in the June 4 guidance. And the language roughly maps to the terms must and should from the June 4 guidance, and that's how they're translated into yes or no, which is the required categories, and the requested is the should.

We also expanded the ask on order entry questions to include optional value sets. And the intention of doing that was to make those questions a lot more useful-- the answers to those questions, I should say, a lot more useful-- by providing increased granularity on what are the actual responses beyond yes and no.

The expanded AOEs, ask on order entry questions, are listed as optional. And they're optional because they were not required and not listed in the June 4 guidance at that level of detail. So the general expectation from laboratories is that the order of priority for implementation and building out the IT systems to capture and transmit these data sets are to focus on the required data elements first. Those really should be coming in starting now.

Once those are nailed down and those are being reported pretty well or seamlessly in your lab, we would like you to move on to the requested data elements. And again, I know some folks were already ahead of the game, even ahead of August 1, in recording those. And then move

on to the optional fields. One of the ask on order entry questions became optional in its entirety, and that's the first test question.

Throughout the process, over the last couple of months in developing a more technical guide, we've worked with a lot of stakeholders and gathered a lot of feedback from folks on what they're experiencing as technical challenges, logistical challenges, and coordinating type challenges between clinical providers and laboratory communities, and so on and so forth. The take home message in all of those discussions is that we have a very heterogeneous laboratory network and laboratory entities in the country. And so folks are definitely at a different place with regards to IT readiness for implementation. And we do understand that. It would be unreasonable to expect that every single lab is technologically ready at the same place and time for all of these data elements.

So we certainly understand that, and we very much appreciate all of the effort that is going into the capture of high quality comprehensive data sets for reporting at every level. This information will help guide the response all the way from the entire national response down to the individual-- patient and clinical care of individual patients. So we thank you all so much for the hard work that I know has already gone into this, and we will continue to go into bringing all these elements online for reporting purposes.

I think those are some of the high points, and I'd like to turn it back over to the other speakers. I'd stay on, of course, to answer any questions if we have time at the end. Thanks so much, Jasmine.

JASMINE CHAITRAM: Thank you, Sara. We did get a couple of questions. I'm going to actually ask them now. The first one I'll answer. It was a question about which table are you referring to. And so what I'm going to do is I'm going to put a link in the chat box to a LOCS message. This is an email that we send out-- Laboratory Outreach Communication System. I've mentioned it before on these calls. And it provided links to the table that was posted last week with the implementation and technical specifications that Sara was just speaking about. So all of you can look for that in the chat box and it will take you to that message.

The questions that we received, we've got two right now. The first one, all of the AOE questions in the [June 4 guidance](#) were described as requested, not required. Has that changed?

SARASARA BRENNER: No, that has not changed. And the table they are also listed as requested with the exception of the first AOE, which was first test, yes or no. That has been changed to optional, which is sort of a somewhat lower priority than requested. So they all remain requested with the exception of first test, which has become optional. And then the additional pieces, the additional values that I mentioned that provide more granularity around the yes, no, and unknown, those are all optional.

JASMINE CHAITRAM: OK. The next question says, since the technical specifications were released less than 24 hours from the compliance state of the lab reporting guidance, is there an expectation that laboratories are to comply with that August 1 deadline?

SARASARA BRENNER: So that's a great question. We get that one a lot. The June 4 guidance was released on June 4 with the timeline up to August 1. So the must or the required data elements are expected to be being reported by now. The technical specifications are meant to support folks in how they're doing that. It would have been ideal to provide this support earlier on, and we certainly do understand that this would have been helpful to have before Friday. Nonetheless, this is when it was able to get out.

So the hope is that if you're not there yet, and you understand that not everybody is going to be there right now, that you use this guide, and reach out if you need technical support or assistance. Reach out to HHS or the DLS email address, and work to onboard these data elements, and streamline them as quickly as you can. Again, focusing on the required data elements first, then moving to requested, and then moving to optional.

JASMINE CHAITRAM: Thank you. So there's one more question, and I had already mentioned this to you, Sara, but just so that folks on the phone can hear it-- there was an error in the SNOMED code for temperature. There was a typo-- 104 versus 100.4. And so just acknowledging that we have received those comments, and maybe, Sara, you could say a little bit about how the table will be updated.

SARA BRENNER: Yup. Believe it or not, no matter how many eyes you put on something like this, things like that slip through. So we appreciate all of your eyes on it and all of your utilization of it as you're working to implement the coding. When you find things like that, and I'm sure there will be instances, please go ahead and send that feedback to the [DLS Inquiriesemail address](#).

We are compiling all feedback, positive, negative, technical, philosophical-- you name it. If you have thoughts on it, please go ahead and send it in. We are compiling that. And we'll probably do a batch update at some point within the first week and then we'll have to evaluate what else is coming in after that. But we will make updates to the table when technical errors are found. So please continue to send.

JASMINE CHAITRAM: Sara, thank you so much for answering all those questions. I don't see any other ones at this time, so we are going to move to our next speaker. So we actually have a group of speakers coming up, and this is from each of the three agencies. We've got a speaker from CDC, Dr. Ren Salerno. We've got a speaker from the Centers for Medicare and Medicaid Services, Amy Zale, and we also have a speaker from the US Food and Drug Administration, Toby Lowe. And all three speakers are going to be giving an update on pooling. Recently, CDC posted some guidance on pooling, and so I will turn it over to our first speaker, which will be Dr. Ren Salerno.

REN SALERNO: Thanks, Jasmine. So this will be fairly quick, because we know that there's still a another presentation as well as Tim Stenzel's answering of questions, which everyone really appreciates. And so we're going to just summarize what is currently available on our web sites related to pooling, but the more detailed information is available. And in terms of [CDC's pooling guidance](#), which has been posted since the last time that this meeting occurred-- so 10 days ago-- you can find it if you Google or search "CDC COVID laboratories". And there will be a button on that page that comes up that says pooling guidance or something similar to that. So next slide, please.

So very quickly, presumably, most of you on this call understand what pooling is. It's the combining of multiple samples into a single test. In this case, we're talking about for the detection of SARS-CoV-2. We also are talking about pooling for molecular PCR testing. And what pooling does is it allows more samples to be tested with fewer materials, potentially increasing capacity.

Pooling is particularly useful when the prevalence of disease is relatively low and the number of positive tests is expected to be relatively low. And what pooling allows a laboratory to do is that if the pool test result returns negative, all those samples can be presumed negative with a single test. If the pooled test result returns positive or indeterminate, each of the samples would need to be retested individually to determine the actual result for each of those individuals. Next slide, please.

So this is just a summary of what you can find in detail in the CDC published guidance. We thought it was important to define diagnostic screening and surveillance testing, and we tried to do that consistently with what appears on the FDA website. One of their FAQs does the same thing. We tried to be clear about the regulatory requirements for diagnostic and screening-- testing when using a pooled strategy, and how that differs from surveillance testing when using a pooled strategy.

We clarify expectations for reporting results to both patients and health departments, which also differs depending on what type of testing you are utilizing, whether it's diagnostic or screening, or if it's surveillance. And then we described some technical limitations associated with pooling. Next slide, please.

I'm going to show three charts that appear at the bottom of our guidance, which tends to sort of summarize some of the concepts that we describe in narrative form in the guidance itself. This is the first of three charts to explain that if you're doing screening, testing or diagnostic testing, you need to be using a CLIA-certified laboratory and you need to be using a test system authorized by FDA or offered under the policies in FDA's guidance. If you're doing surveillance testing, that can be done either in a CLIA lab or a non-CLIA-certified laboratory. Next slide, please.

So this chart describes returning test results to health departments. As Sara explained, all COVID-19-related testing needs to be returned to health departments. But for pooling, it's

really specific to diagnostic and screening testing. And so the negatives from a pool test and a diagnostic or screening testing scenario would be reported individually to the health department. Obviously, we don't want you to report pool test results that are positive or indeterminate because those positive or indeterminate pools need to be retested individually before they are reported to the health department.

In terms of surveillance testing, because surveillance testing is on de-identified specimens, there's really not much value in returning those results to the health department, because the health department can't follow up on results that are not identified or linked to an individual. However, we know that surveillance testing results are often requested by an institution, and in those cases, those results can be returned in aggregate to the requesting institution, which could be a health department or could be a university or whoever is sponsoring the study. In that case, again, the negatives should be reported as presumptive negatives. Next slide, please.

And when it comes to reporting to individuals about pooled testing, it's important to emphasize that surveillance testing should not be specific to individuals. And so there would be no need or ability to report surveillance testing results to individuals. And for screening and diagnostic testing, negatives can be reported to the individual or the individual's health care provider employer according to the instructions for use. And depending on the device that you're using, there may be specific language that needs to accompany a negative test result from a pooled strategy.

And then obviously, for positive or indeterminate results, those should not be reported to an individual, because they need to be retested individually before a result can be returned to either an individual or a health care provider or employer. So that's it for me. Very quick summary. I think the next slide, I get to turn over to my colleague, Toby Lowe, at FDA.

TOBY LOWE: Thanks, Ren. So for anyone who doesn't know me, this is Toby Lowe. I am associate director in the Office of In Vitro Diagnostics at FDA. And just to talk through some of the information that we have available about pooled testing, starting with the EUA templates, we did just update those recently to include additional information in the molecular diagnostic templates about pooling. So they include information on our recommendations for validating adding pooled to an existing previously authorized test as well as to including pooled testing in your initial validation for an ocular diagnostic test.

That includes validation recommendations both for specimen or sample pooling, where you pool the transport media as well as swab pooling, where you would add multiple swabs to a single transport media.

And then in those templates, the links on those slides lead directly to the templates, and then they can also be found on the IBD EUA page, which is the last link on this slide.

And then the FAQs that we have, we have a number of FAQs that discuss concepts related to pooling. The first one, as Ren mentioned, discusses the difference between surveillance,

screening, and diagnostic testing. And then there is an FAQ that talks about the use of diagnostic tests in symptomatic versus asymptomatic individuals. And as I know, we've discussed previously, a variety of calls, a lot of the tests are currently authorized for use in individuals suspected of COVID-19 by their health care providers. And from FDA's perspective, that can include both symptomatic and asymptomatic individuals, where there is a reason to believe that they may have been exposed or may have been infected. And that is at the discretion of the ordering health care provider.

The next FAQ mentioned here is about screening. So we have authorized a couple-- or maybe just one at this point-- tests specifically for screening of asymptomatic individuals without an exposure. And so we also do have recommendations for validating tests for that indication in the templates that I just mentioned.

And then the next question is specific to pooling and discusses some of the information that we have in the pooled discussion and the templates about validating tests for pooling. And it's important to note that-- I'm sure many of you are familiar with the policy we put out about notification, where labs notify the FDA that they have developed a test, and validated it and begin testing, and then submit their EUA for FDA review after that.

And it's important to note that policy also applies to tests that are using single pooling. So if you have developed a tester or modifying test to sample pooling, we recommend that you look at the validation in our templates, and then you can go ahead and notify us, and begin testing while you review the EUA.

And then lastly, there's a FAQ noted there about using tests for surveillance. And as Ren mentioned, FDA does not generally regulate use of tests for surveillance purposes. That would be outside of FDA's peripheral, generally. And then the last thing here on this slide just goes to the IBD EUA page for COVID-19. And we have added a designation for going on the table on that page so that you don't necessarily need to click through each authorization to determine which tests have been authorized for pooling. I believe there are two or three right now that are authorizing pooling, and we expect there to be one more coming soon. So with that, I will turn it over to my colleague, Amy Zale, from CMS.

FDA Molecular Diagnostic Template for Laboratories

AMY ZALE: Hi. Thank you, everybody. I want to take the opportunity to just say thank you for being included in this discussion today. And so from the CMS perspective, we just wanted to highlight for everyone that we have an FAQ document that is found on our website. And the link for that is here on the slide. I can also put it in the chat so it's a little more easily accessible if that is helpful.

And for surveillance pooling, the biggest thing to remember from a CLIA perspective is that facilities that are performing SARS-CoV-2 surveillance testing using a pooled sampling procedure to report non-patient-specific cohort results will not require a CLIA certification.

However, if at any time a patient-specific result is to be reported by your facility, you must first obtain a CLIA certificate and meet our requirements to perform testing. Please let me know if there are any questions. And again, we would refer you to the link that is on the slide and then I will put in the chart for further guidance on CMS policy on this topic. Thank you.

JASMINE CHAITRAM: Thanks to all three of you so much for that information. I do have a few questions. I think the first one can be answered by Ren. It's, what is the maximum number of samples that can be pooled?

REN SALERNO: So our guidance does not specify a maximum number of samples. I think from our perspective, pooling is a self-limiting methodology. And obviously, it depends on disease prevalence, it depends on the sensitivity of the assay that you're using. But in general, the larger the pool the more likely that you may not be able to return a negative result and you'll have to do more testing. So in general, the pools need to stay pretty small. But I think that will depend on a lab to lab basis. It'll depend on the prevalence and the assay.

JASMINE CHAITRAM: Thank you. The next question is, is there a requirement to test positive pool? I think that's getting to if there's a positive in the pool, what's the requirement for retest?

REN SALERNO: Yeah, so this is Ren. And I saw a question about matrixed pooling. I might have to let Toby do this, but a couple of the EUAs on pooling that were approved or authorized came out after our guidance. And depending on the authorization, there may be different methods that are allowed. I don't know, Toby, if you wanted to cover that.

TOBY LOWE: Sure. So there is a requirement to be able to confirm where the positive sample in the pool came from. So you can see in the authorizations for the simple pooling is a reflex to test the entire pool for the matrix pooling. And it's based on whether we can deconvolute it using their matrix strategy.

JASMINE CHAITRAM: Thank you. The next question is are physician laboratories allowed to do pooling of samples in the clinical setting? Pooling would not be in compliance with the test manufacturer's package insert. And I think this is getting to physician labs doing waived testing and whether or not they can do pooling.

REN SALERNO: Toby, do you want to take that one?

TOBY LOWE: Sure. And Amy, feel free to jump in. Right now, the tests that have been authorized for pooling are not authorized for use in a waived setting. So I will defer to Amy to weigh in from the pool perspective on those labs' ability to deviate from the instructions we use.

AMY ZALE: Thanks, Toby. So for any laboratory who modifies the instructions for use, which include intended use, for an EUA, that testing would default to high complexity testing. And then so therefore, the laboratory who was actually performing that testing would need to meet

the requirements and have the certificate that met the requirements for high complexity testing.

JASMINE CHAITRAM: Toby, thanks-- to both of you for answering that one. The next one is, are surveillance results less valuable since they are not performed in a CLIA lab?

REN SALERNO: So this is Ren. I wouldn't say they're less valuable. Surveillance testing has a different objective than diagnostic testing. Surveillance testing is intended to understand what's going on at a population level, to guide population level decision making and policy making.

But surveillance testing can be extremely valuable and extremely important. But I think the difference that we're trying to articulate here is that diagnostic testing is specific to an individual patient that allows for medical decision making and specific follow up by the public health department in terms of contact tracing and transmission prevention. And so therefore, you know we look at the results of diagnostic testing a little bit differently than we look at de-identified results from surveillance testing.

JASMINE CHAITRAM: Thank you. We did have several more questions, but in the interest of time, I'm going to move to the next speaker. And we'll try to answer some of these other questions about pooling after the call during the week. And so thank you to Amy, Toby, and Ren. Our next speaker is Bev Dickson. She is from the Texas Health Presbyterian Hospital. And she's going to be talking about risk assessment. And I'm very grateful for her for doing this presentation, because I know that many of you have asked for a presentation on risk assessment. So hopefully, this will be everything you're looking for. Bev?

BEV DICKSON: Can you hear me?

JASMINE CHAITRAM: Yes, I can.

BEV DICKSON: Great. So today, I'm going to basically describe a risk assessment that we did in the age of COVID. And I'm sure everybody familiar with the basic objective of biosafety, which is containment. And one of the ways we do that or one of the tools we use is risk assessment. So we're going to talk about what we did in relation to a biosafety discussion regarding the safety of sending clinical specimens through the pneumatic tube during the COVID epidemic. Next slide.

So I'm sure you know that there are many different templates that are used for evaluating risk assessment. But basically, it's a systematic process of gathering your information, evaluating the likelihood, the consequences, and the risk control measures that could be used to reduce risk. This is just one template from the Uppsala University web portal. They're all very similar. And you describe what the work is, identify risks, determine whether they're acceptable or not. If not, what can you do to enhance safety. And if they are, you can go ahead and do the work you wanted to do, but you would need to monitor and trend, and then re-evaluate. Next slide.

So this is a little bit more of a simplified risk assessment tool that we use. In this particular case, the steps were modified somewhat. And the steps are similar in all of these templates. You explain what the situation is. In this case, it was, can we safely send possible COVID specimens through the pneumatic tube. Step two would be to provide background information. Step three and four, to provide either support of or opposition arguments to the process that you would like to implement. Next slide.

So in this particular case, we used a format to start the thought, to initiate this, which is probably fairly common in community hospitals, because it's used by nursing for communication to their team. And this is called the SBAR. It includes the SBAR, meaning situation, the background, the assessment, and the recommendation.

And so the initial communication that went out was an SBAR communication. And you can see that the situation was we are going to need to assess the risk of sending assessments through the pneumatic tube system during the COVID pandemic. And in this case, our hospital is a tertiary care hospital campus. The pneumatic system is very vital to us providing timely turnaround time for three different hospitals. And providing efficient workflow for our diagnostic care.

The published guidelines at the time when we were making this determination were discordant. The CDC initially just advised specific risk assessments be performed. And the WHO recommended against the use of the pneumatic tube system. Today, the CDC has a slightly different advice on their website, which you can get to by going to CDC.gov. In the meantime, we were trying to determine if blood, urine, and respiratory swab specimens could be routinely transported on inpatients and ED patients, and risk assessment ensued. Next slide.

So step two included getting background information. So we perused the articles, of which there were many being placed online, concerning viral load in different types of specimens. And also, information regarding the safe use of pneumatic transport, what types of engineering and mitigation controls are in place in these different transport systems. And also, investigating our particular system that we had, because different pneumatic tube systems have some very different engineering design. And so all of these things were used in the background information gathering. Next slide.

So step three and four was to build the case. So this is our evaluation. So these are the main points. We determined that our covered specimens swabs, our respiratory swabs, were submitted in screw Top tubes with a maximum of 3 CCs, but most of the time, 1 to 2 CCs of transport media. Screw top tube being less likely to pop off or come undone during transport. The specimens were transported with secondary containment, and this was an enhanced control.

We added biohazard bags times two instead of one. So it was an enhanced control. The bag specimens were decontaminated prior to tube transport. And our tube carrier, which we would consider to be the tertiary container, was the durable plastic with rubber gaskets that were

unlikely to allow spillage of the small amount of media that was present. And the fact that it was also enclosed in two bags would make it very unlikely.

Our tube carrier was a snap closure. Less risk of opening on arrival to the lab. The transparent tube could be visually inspected before being opened. The lab people are gloved and masked when they're at the tube's entryway. Respiratory specimen from the background article information. It was revealed that there was much lower viral load, for instance, in blood and urine, thus making the risk minimal.

Tube carriers were being periodically wiped down with a suitable EPA disinfectant that was enhanced controlled. Historically speaking, we had never had, as far as we knew, any aerosolized disease from either transporting TB specimens or influenza specimens or any other type of specimen. In this case, including some accidental Ebola specimens before we knew the patient had Ebola.

Historically, leakage was pretty much confined to urine cups, which were no longer acceptable. So we determined that we felt that this was probably an acceptable method of transport. And that we could also track trends and monitor this by using our biosafety reliability learning tool, and also, that we could use our bloodborne pathogens policy for any exposure, should they occur. Next slide.

So we used this matrix, which is a little simpler in appearance. We basically put in the probability of how often we would think a leakage or spillage could occur into the tube. We felt that was rare. What the severity could be if that occurred, and of course, as we know, COVID can cause death, so we rated that as the highest, life threatening.

And then the detectability how likely was it that we would detect that there had been spillage into the tube system. And we felt that that was very likely. So our risk priority score was 4, with a range of 1 to 64, that each of these is multiplied to provide the score, leaving us with a low risk of having any adverse event from tubing samples in the pneumatic tube system.

The other considerations, actually, during this were two-- the consideration of using the pneumatic tube system. One was the fact that during a pandemic, the likelihood of us losing staff and having less staff, both transport for the hospital, nursing, and laboratory staff to be able to transport these specimens, was a big issue. And so we felt that we would need to be able to use the transport through the pneumatic tube.

And the other thing was that although you sometimes know that someone is a PUI, especially in the case of COVID, there are a lot of asymptomatic and pre-symptomatic patients. And we would likely be sending things through the tube system anyway on patients who had COVID without knowing it. So those were two other things that we were considering when we were looking at being able to use a pneumatic tube system. Next slide.

So the recommendation or the resolution for this post-analysis was that the risk to employees and to the public from using the pneumatic system to transport blood, urine, and respiratory swab specimens was very low due to the enhanced controls and procedures, as well as our historical experience. And that we had a methodology already set up that could track and trend and provide system safety information for our dashboard as long as policies and procedures were for bloodborne exposure and use of the pneumatic tube were updated.

And so this was a kind of a big deal for us. But at the same time, it was a risk assessment that was done utilizing some of the nursing tools as well as close to the regular risk assessment matrices. And that's what I have.

JASMINE CHAITRAM: Thank you so much, Bev. I'm not showing any questions specific for you, so I'm going to move to our last speaker. But if any questions come up, I may throw them in there if we have a few minutes at the end of the call. But thank you so much for that great presentation and for being on the call with us today.

Our last speaker is Tim Stenzel from the US Food and Drug Administration. And Tim is on and sometimes, Sara helps with that she's doing multiple roles, to answer some of the questions we received over the last couple of weeks. And so Tim, go ahead.

TIM STENZEL: Thanks, Jasmine, and hello, everybody. Lots of good questions again this week. And I'll try to get through all of them in time allotted. And also some updates that weren't related to pooling. And so Toby you didn't cover those. First is you may have noted over the weekend that we authorized the first semi-quantitative serology test-- actually, two from Siemens. Semi-quantitative, quantitative, and of course, neutralizing antibody serology test, including those neutralizing tests that are called neutralizing or at least correlate with neutralizing. And so there might be a correlative claim for those tests.

And also, there's going to be tests that more directly actually measure the presence of neutralizing antibodies. And we think there will be a growing need for research use of these, but perhaps also some desire to use these to assess the adaptive immune system as we go forward in this pandemic. So we were very pleased to move into the semi-quantitative space for serology. That's kind of the first steps along this pathway.

Second, in addition to the pooling updates, to the templates that Toby mentioned, we also updated two templates-- one for lab, one for kit developers, for the validation of multianalyte respiratory panels. We see that as important as we move into the fall respiratory season, and some of the symptoms at least of other pathogens will overlap that with SARS-CoV-2. And also, the ability to test multianalytes should preserve things like swabs and transplant media, lab personnel, and space on the instruments. So we see that as an important update to the site going into the respiratory season.

And then finally, for our kit manufacturers, we did make our recommendations for validation of point of care tests. Recommendations clear. Of course, for antigen tests and for actually,

serology tests, we had the point of care recommendations already. And so we just also updated the molecular template for that. And then Toby and others helped us with FAQs for all of those updates, as well. So you can see the templates or check the FAQs on our EUA FAQ website.

Also on Wednesday last week, we provided a template for what was previously called home testing. We now call it non-laboratory testing, because it may not occur just at home, but also can occur at places like schools and workplaces and other non-lab settings. So that was an important update to provide recommendations for validation of those tests. And there's a number of those that are in development, and we look forward to the first reauthorization of a non-laboratory use test.

With that, I'll go into some questions. So first off, there were some questions I saw on the chat that I thought I could weigh in, as well, perhaps. There was a question about what was the recommended pool size for pooling. And Ren did a good job with that. I would just say that the template that we updated for molecular, both labs and kit, does include some additional information about optimal pool sizes. So if you want some help in selecting which pool size works best for you, we have a table that relates to the present positive you're seeing with the efficiency gained and the maximum efficiency pool size.

So you simply go down the table for whatever your percent positive rate is, and you can select the maximum efficiency. Of course, that's the efficiency that you gain from pooling and reduce at least some of reagent uses for pooling.

When we look in the EUA submissions for pooling, of course, pooling is a notified pathway for regulatory for both kits and for labs. You can simply validate, notify the FDA, and then have 15 days to submit your validation. So there's a couple of different things that we think we found as being the drivers of performance characteristics of pooling. Hopefully, this kind of information is helpful to those who want to pool to increase the throughput of their labs.

One is we look at what the overall percent positive agreement is for whatever pool scheme that you choose. Say you're choosing a five pool, a five sample pool where you want to validate, can you detect one positive in a background of four other negative specimens. We do look at the PPA as needing to be at least 85% or greater for that.

And there are a number of drivers of your ability to hit that 85% or greater. One is limited detection of the actual assay that you're using, whether that's your own LDT or that's a kit. And obviously, the lower the LOD, the more likely you are to more easily detect the low positives. And of course, all pooling schemes essentially are going to miss some low positives. So it's important to know what the risk is for you missing-- what is the percent miss rate, basically, for little positives that your labs are going to see.

And so obviously, the other factor besides LOD, the very sensitivity of the test analytically, is also, what is the percentage of very little positives that you see in your lab. And that can vary greatly from lab to lab. And you can imagine if you have only high positives in your lab pooling,

will work really well, because high positives are more easily detected in a pool. And if your percent positive rate is low enough, you can have a fairly high pool and still detect most, if not all, of the samples in your population.

Or if you're at the other end of the extreme, and you have a lot of low positives, pooling may be less ideal for you, because you may miss a lot. So we've seen some pooling schemes even as low as 3 to 1, but since they have very high percentage of low positives, they missed about 25% or more of their positives when they pooled relative to testing these things individually. So those are what we think are the important factors in determining the pool strategy that you have that you want to deploy for your own situation.

Also, I want to let you know that we're working with a number of key kit manufacturers who are interested in adding pooling to their instructions. And obviously, once they do that, it'll be a lot easier for labs to adopt, because they simply follow the kit instructions, and they don't have to do their own full validation. You may want to check whether that's working for you. But probably enough on pooling.

Going to the next question. So if an EUA lists an instrument, but not specific models or versions of that instrument, are bridging studies required? So I would check with the kit manufacturer. If they don't specify, there may be a reason. You just want to make sure that they're supporting the instruments that you use.

If you have an instrument that isn't supported by the kit manufacturer, and they haven't done any sort of validation or assessment of the use of that, then of course, it makes sense for a lab to validate that additional instrument.

We do not require an EUA submission for a new instrument. But do expect that the validation will be done, and that that validation shows a high concordance to a model that may be included in the package insert. Second is do you know of any labs that have done a bridging study. And in this particular case, we're asking about Chi cube, HT, and the CDC EUA COVID test.

I'm not personally aware. However, I would refer you to the manufacturer. Often, they are working with labs and we encourage them to work with labs update the reauthorization for their own tests with new options. And we encourage them to work with labs and are open to the use of clinical lab data to support an update to the manufacturer's kit. So we do encourage those kind of interactions between labs and kit manufacturers. We're kind of all in this together, and the more we can help each other, the better we'll all be.

The next question had to do with viral and activation steps. And I asked a follow up question of Jasmine and got a little bit more detail. So the question had to do with the Thermo Fisher system looking at bringing in the new COVID test system for high volume testing. And we noticed that it required the samples be deactivated. And they're currently using some other manufacturers' instruments and that don't require this treatment.

So my recommendation is to follow the manufacturer's instructions for the samples that you run on the particular systems. Presumably, they did testing to validate these different procedures for each of the kits and development by the developers. And if you were to go off label and follow instructions for one kit and apply it to all the testing in your lab, there could be a deleterious impact on performance and characteristics for those other kits.

So in particular, say in heating activation, there is the risk that it could degrade the RNA target. And depending on what the buffer is that is used do that inactivation in. So again, I would refer you to the kit manufacturers for that type of change or situation.

There was another inactivation question about point of care molecular tests such as the GeneXpert. And again, I would refer you to the kit developer to Cepheid for their thoughts about inactivating samples prior to use on their systems. I know that there were a lot of questions circulating about for the Abbott m2000. In my direct conversations with Abbott, and I would defer to your own conversations with Abbott, they kind of were dissuading the use of inactivation. However, there may be lab situations where that's important, so I would defer to local questions and concerns and work with the developer.

Let's see. And I think that is the end of the questions.

Thank you, Tim. Thank you so much. We are out of time. And so for that reason, I'm not going to ask you any more questions, even though we did get some more this week. I'll send those to you guys. Thank you to everybody for participating in today's call. Thank you to our panelists for putting together great presentations and answering questions. Our next call will be on Monday, August 17, at 3:00 PM. And if you are not receiving announcements about our calls, please send us a note at LOCS@cdc.gov, and we will get you on our distribution list to receive information about our calls. Thank you, hope everybody has a great afternoon, and stay safe.