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.

Cut to Pooling Presentation

JASMINE CHAITRAM: 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.