Clinical Laboratory COVID-19 Response Call

November 2, 2020

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JASMINE CHAITRAM: Hello, everyone, and thank you for joining the Clinical Laboratory COVID-19 Response Call. The Division of Laboratory Systems at CDC has been hosting these calls since March. I'm Jasmine Chaitram, the Associate Director for Laboratory Preparedness in the Division of Laboratory Systems at CDC.

And just as a reminder, DLS-- the Division of Laboratory Systems-- has been supporting clinical and public health laboratories before COVID. We've been engaged in a number of different topics-- things like quality and safety, workforce development, training, informatics, biorepository science, as well as data science. And we were also doing preparedness and response activities, and we continue to do those through the COVID-19 response and serve as a liaison between the public health and clinical laboratories and the CDC Emergency Operations Center. We've been hosting these calls and hope they have been helpful to you.

Today's agenda is showing on the screen, and we've got a few speakers. And I'm going to cover a few of our normal housekeeping items before we have our first speaker, so just a couple of reminders.

The first one is that our next call will be on Monday, November 16. We've been hosting these calls every other week now, from 3 to 4 PM Eastern time. And we continue to ask for your input, especially on training and workforce development. If you have any specific needs, please email them to LabTrainingNeeds@cdc.gov. And this is related to training and workforce development.

As a reminder, we also have links that are helpful information to the clinical laboratories, and we keep them on our slides-- which we also post our slides to the DLS website. So after the call, if you want to go back and find any of these links as a resource, you can go to the slides-- which are posted along with the transcript and the audio for these calls. And the information is now

found on the CDC Preparedness Portal, which DLS hosts as a one-stop shop for all of our information that we have available to the laboratories. So our LOCS messages can be found here-- that's the Laboratory Outreach Communication System-- as well as the transcripts for our calls.

We also recently posted guidance for point-of-care testing. Please get the word out on this page, especially for those testing sites that are not traditional laboratories, that are using these types of tests, that need this information.

And then finally, a reminder about asking a question. The Q&A button in the Zoom webinar system is the best way to submit a question to us. We don't really want those questions coming through the chat, because then they're not recorded. We do try to answer as many questions as possible during the call, but because of the number of people that are calling in and submitting questions, we sometimes don't get to answer all those questions. It's really important to put your question in the Q&A along with an email, because we will try to get back to you after the call and provide an answer to your question. We also use this information to help us with preparing agendas for future calls, so we really want to have a record of what those questions and concerns were.

And then also if you're the media, please use media@cdc.gov to submit your questions to CDC, and if you're a patient, reach out to your health care provider.

And with that, we are going to move to our very first speaker, which is Sarah Harding from the Centers for Medicare and Medicaid Services, and she's going to be talking about CMS reimbursement.

Sarah, you ready?

SARAH HARDING: Yeah, absolutely. Thank you very, very much for having me on today.

I believe that some of the impetus for having me on today was a recent administrators ruling that came out a couple weeks ago. And so I will talk to that specifically. But first, I just wanted to kind of give a very broad overview of where things are kind of at this time of the year, with reimbursement for new codes, and new tests that may be coming on the market that are looking at COVID-19. Basically, at this point in the year, if a new test is developed and gets a new code from the C-- from the AMA CPT committee-- that code, as far as payment and coverage, will be evaluated at the local carrier levels.

So I don't know-- and I say this mainly to one of the first questions on the Q&A is looking at new tests. And I would say that if you have questions about specific new codes, the first place to check is going to be with your local Medicare administrative contractor. They will be setting payment rates, largely, for any new tests.

And the reason that is, is that there isn't a national effort for payment rates at CMS until the summer of each year. So there were a few tests early on in the pandemic that made it into our public meeting, which occurs in July. And so those were discussed at that meeting. But otherwise, anything that missed that deadline now is just dealt with at the local level. But you can still always send us questions and comments about any new test that might be coming out, but that will probably be our answer.

But in terms of what I was asked to speak about today-- and then I will look, I do see a few of these Q&As coming in, and will try to speak to them as well-- but the new administrators ruling that came out the middle of October created a new add-on payment for COVID-19 diagnostic tests that are run on high throughput technology. So an original administrator's ruling in April established two HCPCS codes for molecular COVID-19 testing tests that were performed on high throughput technology. And the definitions of all of this are in the rulings, but basically these created two new codes-- U003 and U0004. And these were both reimbursed, originally, at $100.

The administrators ruling that came out a couple weeks ago changed that rate. It decreased that rate to $75, but it established this add-on code-- which is U0005-- to basically add $25 to tests that meet two individual criteria. One is that the test is performed in two calendar days or less from the date of specimen collection, and two is that the majority of COVID-19 diagnostic tests using the high throughput technology in the previous calendar month-- so for all payers-- were also completed in two calendar days or less.

So this was meant to try to speak to some of the timeliness of these tests. Really wanting to make sure that the results are of most value to patients, and trying to encourage as much as can be done to turn those results around so that people can act on those results, whether they're positive or negative.

Now I know one of the questions we have gotten already has been to clarify the “two calendar day” time period. And so I wanted to just say we haven't-- we are working on publishing several frequently asked questions that will follow up on this ruling. And so I think that will help some of the confusion, or some of the clarification needs.

But I can say here that the intention of the two day calendar limit was basically to look at the very first day that the specimen is collected as a day zero. So if a specimen is collected on a Wednesday, that's your day zero. Thursday is day one. The end of Friday would be the end of day two, so that add on payment could be applied if the test is completed-- which means results are ready to go by the end of the day Friday.

Now again, please don't record me saying that and hold me to it, because I believe that there are going to be FAQs published that you can point to much better than my voice here. But hopefully that will help that clarification there.

So I'm looking through some of these Qs and As. I don't know to the speakers to, or to the organizers-- do you want me to look at these Q&As now and try to speak to them, especially if my name is in them? Or do you want to wait until the end of the call?

JASMINE CHAITRAM: Thanks Sarah, this is Jasmine. It would be great if you can answer some of these questions now. But if you would please read out the question that you're answering, so that way we know which one you're responding to specifically. Because we really do try to be responsive to these questions, either on the call or later. And so if you-- I can either read the question to you, or you can read the question out loud and then provide an answer. Your call, since you're able to see the questions.

SARAH HARDING: OK, yeah. I'll give it a try, and-- but I won't go much more over my time limit, because I know there are other speakers. And I am very happy to respond by email after the call to any other questions that we don't get to.

One question asks, will pooled testing with an EUA be reimbursed? So and that's-- I love this. So I think someone else is going to answer that question, which is great. So stay tuned.

This question is for Sarah. When Congress passed the CARES Act, it appeared to limit reimbursement to only those COVID-19 tests that were in the process of being submitted for an EUA, were under an EUA, or were regulated directly by a state. I think there are eight that assumed this responsibility. Now that FDA no longer requires an EUA for a COVID-19 laboratory-developed test, would a new COVID-19 19 LDT not under an EUA still be reimbursed by Medicare?

So again, I think that question first and foremost is for the local contractor to give an ultimate decision on. But typically tests that are paid for by Medicare do not require FDA approval. So there are programs that certainly look to FDA approval, but on the CLFS-- on the Clinical Laboratory Fee Schedule-- are plenty of tests that are not FDA approved. And obviously also do not have an EUA, since that is typically in an emergency situation.

So that does not guarantee coverage by any means. So once again, I would encourage you to speak to your local contractor. But I would say, simply speaking, the lack of an EUA would not prevent payment by Medicare.

OK, yes. So the question this-- we have been hearing this. I did check with my local payer, and they said they were waiting for guidance from CMS-- ooh, it jumped. To-- it-- sorry, this jumped out of my pit, but basically they were-- here we go-- to set rates for the new codes. It seems like a catch-22. Yes, it does seem like a catch-22. I agree with that sentiment. The process is indeed for the local carriers to set rates. And so that is not wrong.

I think what local payers have been sort of looking to the national office for is kind of a go ahead to publish those rates. And I think some of it has really just been in the context of just wanting to make sure everybody's on the same page, all the ducks are in a row, and you know--

because there have been situations of administrator's rulings, of IFC, of interim rules, of other rules. So there's just been so much going on in this pandemic. I think what you're seeing is just wanting to make sure that things are lined up correctly.

So it is a catch-22, but it's also a catch-22 where neither side is necessarily wrong. But you're also-- Dr. Aida, you are not the first person to ask this, but I appreciate you bringing it up again. And I will do what I can to make sure that all of our local payers are ready to go. So thank you though for that.

Can providers refuse samples because it will lengthen their turnaround time? That is an interesting question that I would certainly-- I would need to look into. From my perspective, I don't think I can answer that here and now without looking into that. But I will take that back. That is from John Weiss-- can providers refuse samples because it will lengthen their turnaround time?

OK, so all right. I'm going to try for one more, and then I will turn it over to other speakers, if that's OK. And then I'm happy to stay on and try to answer more.

So this is from R. Schulman. So regarding the recent announcement starting in 2021 Medicare will pay $100 only to labs that complete high throughput COVID-19 diagnostic tests-- within two calendar days of the specimen being collected-- and labs that take longer than two days will be paid $75. The questions are, one, since it appears that policy will be enforced primarily by audit or medical review, will see CMS issuing any guidance on how a laboratory should demonstrate compliance with this requirement? That answer is yes. That will be coming out in FAQs on what kind of review-- not the kinds of reviews, but the kind of paperwork and recording of that information you would want to keep in case of review. So yes, guidance is coming.

And number two, if a hospital collects patient specimens and sends them to a commercial laboratory for high throughput COVID-19 testing, can the hospital bill Medicare for HCPCS code 0005, since the hospital did not actually conduct the test? How would the hospital be able to demonstrate compliance in the event of an audit or medical review, since it would be the commercial laboratory that would have the records necessary to demonstrate compliance with the requirements for use U0005? So again, I think what-- I'm going to, I will make sure I record that specific question. But I believe the guidance that is that we are working on now will speak to this, and basically try to help out how that can be recorded and collected so that it can be noted, if needed.

Now I do not, however, know the answer on whether the hospital itself can bill for the add-on payment. That I will also take back and look into, and perhaps think about generating some further guidance on that issue. But if not, I have your email address at the top of the question. And so I can get back to you directly.

So thank you very much. I think I will stop there, but again, I'm very happy to take more Qs and As after, at the end of the call.

JASMINE CHAITRAM: Thanks, Sarah. I'm going to ask you the one question that did get lost in the shuffle, but will pool testing with an EUA be reimbursed was the question.

SARAH HARDING: OK, so that was for me. OK, good, I wasn't sure.

So typically speaking, at least-- so this is a tough question, again, from a Medicare standpoint, simply because if you're pooling the samples you know they're not specific to any one beneficiary. And I think the understanding is, typically, a pooled sample is going to be more for a surveillance purpose rather than diagnostic. Now again, I know that's not going to be true in every single cir-- in every single circumstance, but largely speaking, if you have your pooled samples and they're all negative, you're not going to run them again. If you have the pooled samples and one is positive, then you would run them all to the specific beneficiary. And that's going to be kind of a much more clear circumstance where Medicare would pay for those.

The pooled samples, however, again I think, largely speaking, since it's not in a diagnostic frame-- again, it is a question for your local contractor, but my understanding-- and I'm also not on the coverage side of things, so forgive me if I'm speaking out of turn. But that is my understanding, is that from that initial pool perspective, it would not be it would not be covered by Medicare.

JASMINE CHAITRAM: Great, thank you. So Sarah, if you're going to stay on the line, if you wanted to answer any of the questions that have come through the Q&A feature you can just click "type answer," and everybody will see the response there. So that's your call on whether or not you have a response that you'd like to provide for some of the questions that have come through so far. But thank you so much for taking the time to be on the call with us today. We really do appreciate it.

SARAH HARDING: Anytime, thank you.

JASMINE CHAITRAM: So we're going to move to our next speaker today, Daniel Rhoads from the Cleveland Clinic. He's going to be talking about Ct-- cycle threshold-- values, and the caution that should be used when interpreting those. Daniel.

DANIEL RHOADS: Thanks, Jasmine. I want to thank Dr. Nancy Cornish for reaching out to me and Dr. Bobbi Pritt. We and others on the College of American Pathologists Microbiology Committee wrote a letter to CID, and at the end of this short presentation I'll discuss some of the cautions that we've voiced in that letter. Next slide.

So this is the virus that we're all talking about, right? So at the top you can see the genome stressed out, at the bottom you can see the different proteins on the outside of the viral particle. Next slide.

So different primers and probes can be designed to target the genome in different areas. This was published early on in the pandemic, and you can see lots of different areas of the genome can be targeted with these primers and probes. Next slide.

This is just a reminder of what we're doing when we do PCR right. We start with a template in the primary sample, that's there in green, and then there-- and then there are nucleotides in blue, and primers in red. And every time one cycle occurs, ideally we double how much target, or how much amplicon is in the specimen, or in the samples, so that we go from one copy to two copies to four copies. So as the PCR cycles, more and more of the target is created. Next slide.

So at some point, when the target crosses the threshold, they're depicted in that red line. The fluorescence crosses the threshold, and we call a sample positive. So if there's a lot of target in the primary sample, then it takes fewer cycles to reach the point where that fluorescence is detected.

So you can see there on the left, the green. That presumably had a lot of target, relatively speaking, in the primary sample. And then all the way on the other side, that blue gray. That presumably had less target in the primary sample, and it took a longer, or more cycles, until it was able to cross that threshold. So maybe that green line-- that green sample-- crossed the threshold at about 12 or 13 cycles of amplification, and the blue crossed around 25 cycles. Next slide.

Oh, and if there are any questions I would ask that the program organizers maybe screen those and I'm happy to answer those at the end.

So there's different things that influence the Ct value. So this paper is a nice paper. I try to put QR codes on here so that you could, anybody watching could reach the paper directly if they desired. But this is a nice, short paper describing the correlation of different specimen types and Ct values. And also in the supplementary materials that I am not showing, it talks about positive and negative percent agreement.

But on the left, you see the provider-collected nasopharyngeal swab versus a patient-collected tongue swab. And so there is more target, presumably, in the NP specimen collected by the provider than the tongue swab collected by the patient. And that's demonstrated because there are lower Ct values in the specimens that turn positive from the NP swabs collected by the health care workers versus the patient-collected tongue swabs. So it took longer to turn positive for the tongue swabs than for the NP swabs.

And then there's other specimen types here. There's the nasopharyngeal swab versus the anterior nare swab, and then on the right, the NP swab versus the mid-turbinate swab. Next slide.

So a group out in New York put together this nice paper in CID-- Clinical Infectious Diseases-- and they describe that in-hospital mortality is related to the Ct value for SARS-CoV-2 at the admission time. So what they found was lower Ct values, which means higher viral burden in the specimen, correlated with worse outcomes, or higher mortality.

So notably, they used NP swabs and universal transport media. They looked for the open reading frame 1ab target using the Roche 6800 assay. We'll talk about that more in the next slide or two. And they found that low viral load-- as they described, it meaning high Ct values-- resulted in higher survival, whereas higher viral load-- or lower Ct values-- correlated with higher mortality.

So this paper and other papers are definitely interesting and relevant to clinical practice. And providers read these papers and get excited and want our laboratories to rapidly implement these interesting findings, and potentially report Ct values, so that that can help them potentially manage their patients. Next slide.

This is a very busy figure with a lot of data in it. I would like to focus on that wiggly black line going from top left to bottom right, across the figure. So that the percent of specimens that were able to be cultured for SARS-CoV-2, or the culture positivity rate correlated with the Ct value. So all the way on the left with very low Cts-- Ct values of 11, 12, 13-- they were able to recover virus by culture in all of those specimens. And you can see as the Ct value increases, as the amount of virus in the specimen decreases, the likelihood of recovering SARS-CoV-2 by culture decreases.

Notably, things with very low Ct values, very high virus-- in the teens-- some of those are not recovered by culture. So mid to high 80s are recovered by culture. And then at the other side of the figure, specimens that tested-- or that crossed the cycle threshold in the 30s, they oftentimes were not recoverable by culture. But maybe 10, or 15, or even 20% of the time, they were able to be recovered by culture. So this paper does a nice job demonstrating that Ct value correlates with in vitro infectivity of a specimen, but it's not absolutely predictive. Next slide.

So this is some of the points from the letter that we wrote to Clinical Infectious Diseases as representative of the College of American Pathologists Microbiology Committee. These were some limitations that we wanted to point out to infectious disease providers-- and also the laboratory community-- to just give a word of caution around extrapolating, or trying to over-interpret Ct values. So notably, the FDA-authorized methods have not been authorized for quantitative reporting. They are qualitative assays with positive, negative-- or detected, not detected-- results. And to my knowledge, there is no in vitro diagnostic test available that's quantitative for SARS-CoV-2.

Also keep in mind that not all tests generate a Ct value. Only real time PCR does. So things like nested PCR or isothermic amplification will not generate a Ct value. So that's not even available.

Also, specimen collection impacts the Ct value. So we looked at the specimen type in one of the previous slides-- for example, anterior nares versus NP swab, or a tongue swab. And also, the time from symptom onset to collection impact Ct value. So late in disease, there-- it is known that the viral burden, or the RNA, that's detectable from an upper respiratory specimen decreases late in disease course. Transport media, such as saline versus UTM, or the volume of the transport medium can impact the Ct value. And also, Ct values vary between test systems, between labs, and between targets. Next slide.

So this, again, was published in that letter to CID from the College of American Pathologists, where we describe hundreds of labs results in testing proficiency testing material. They reported that back to the College American Pathologists, and some of the results are summarized here.

So some interesting points from this figure-- expert- for example, gene expert-- there's a three-cycle difference between the targets, at least in this proficiency testing material. So the median for each target on each assay is depicted by a colored dot. Kudos to Dr. Peaper for putting this figure together. So you can see expert there, with the blue and two and the mustard yellow E. You can see that the E gene is detected before the N2 gene.

Also, there's a 12-cycle difference for the TaqPath assay between labs. You can see the range in that R for Thermo Fisher extends 12 Ct values. There's 12 cycle values. So extrapolating between labs, even if running the same tests, the results are not harmonized. They're qualitatively the same, but the cycle threshold-- where it crossed the cycle threshold-- maybe different between laboratories, even when run running the same assay.

And then when looking between different test systems and different labs, that variability increases. So the median cycle-- the median Ct value for Abbott m2000 was 14 cycles different then with Luminex.

So this is all put together to say, just be careful. Don't, please don't try to over interpret a Ct value. I would encourage labs to do their own studies if they want to try to correlate prognosis or outcomes with Ct values. Some things are helpful, but I would encourage those running the labs and on this call not to over interpret Ct values. So next slide.

In summary, Ct values can correlate with prognosis and infectivity, but Ct values are not absolutely predictive of prognosis or infectivity. And as we saw, Ct values are influenced by many pre-analytical and analytical variables. So please, please interpret Ct values with caution.

So that's the end of my slides. I'd be happy to take questions now or later. It's up to those running the show here.

JASMINE CHAITRAM: Thank you. This is Jasmine. Thanks again for the great presentation.

We do have two questions showing for you. One is just a simple clarification, asking about the data that you presented, if the information has been published?

DANIEL RHOADS: Yeah, so it's been published as a letter in CID, Clinical Infectious Diseases. It should be able to be accessible with that QR code on these slides, which I believe will be posted after.

JASMINE CHAITRAM: OK, great. And then the next question-- should the Ct value threshold for qualitative results be reduced, or at least re-evaluated? I'm seeing a lot of 17 to 30, but most EUAs have a threshold of 40 to generate a positive or reactive result.

DANIEL RHOADS: Yeah, I think that's difficult to say absolutely, across the board. I encourage people to start with the goal. What's the goal of testing? Is it to be as sensitive as possible? Is it to detect patients that are super-shedders and might infect other people? So all of the-- starting with the goal is important. And then there needs to be empirical studies to really prove whether or not the hypotheses surrounding the relevance of Ct values should influence reporting or interpretation of qualitative results.

JASMINE CHAITRAM: OK. And then one more. There is no quantitative real-time PCR test for COVID-19. Should labs be reporting Ct values, or should it only be presence or absence-- detected, not detected?

DANIEL RHOADS: That's challenging. I would leave that up to the medical directors to decide, in each laboratory. But I know that there is some pressure from some people to report Ct values, either routinely or on a case by case basis. And I would just encourage those medical directors to consider the College of American Pathologists' letter, which I have discussed here, when making a decision whether or not to report those values.

JASMINE CHAITRAM: Thank you so much, Dr. Rhodes, for being with us this afternoon. We really appreciate your time.

DANIEL RHOADS: Thank you.

JASMINE CHAITRAM: OK, our next speaker-- our last topic for today-- is our regular FDA update. Tim Stenzel is the person who normally gives this update, and he's finally taking some time off. Sara Brenner and Toby Lowe will be covering for him. And I believe they have an update and some questions they will answer, and then if there's anything in the Q&A, I will ask them specifically.

So I'm not sure who's going to go first, Sara or Toby? OK, Toby.

SARA BRENNER: This is Sara. I think Toby was going to take the first set of questions.

TOBY LOWE: Yes, hi. Yeah

JASMINE CHAITRAM: OK, great.

TOBY LOWE: Hi, everyone. I will go through some of the questions that we had sent to us, that I believe came up on the call last time. So I'm just going to sort of walk through these.

We had a question-- if Abbott ID NOW is used for precise surgical testing, is a reflex test required for PCR, or is it at the discretion of the provider ordering the test? And that is at the discretion of the health care provider.

Next question. Is the SalivaDirect test an LDT or a manufactured kit, with respect to FDA cessation from LDT review? The SalivaDirect test is a distributed test, not an LDT. An LDT is designed, manufactured, and used in a single, high complexity, CLIA-certified laboratory, which is not the case for the Yale SalivaDirect test. Any labs that wish to perform the SalivaDirect test should discuss that with Yale, and should perform the test according to the authorized instructions for use.

See, this is a long one. The FDA has informed us that a test we're developing in our lab and will only be used in our lab is not considered an LDT, because we're using a single reagent obtained from an outside company. Is that interpretation correct? Virtually all LDTs use reagents from an outside company-- e.g., secondary antibodies and substrates for ELISA testing. Is there a specific outside reagent that means an in-house developed and validated test is not an LDT?

So there are many in vitro diagnostic reagents and equipment that are purchased in use by laboratories in the tests that they use and develop. And this would include, for example, analyte-specific reagents-- such as primers, and probes, and antibodies-- general purpose reagents-- such as preference enzymes, and-- excuse me-- enzymes, substrates, secondary antibodies, et cetera-- general purpose laboratory equipment-- such as pipette tip and 96-well plates-- instruments, et cetera. And generally, LDTs are tests that are designed, manufactured, and used within a single, high complexity CLIA-certified laboratory. However, tests that are designed in one location, but manufactured and/or used in another location would not be LDTs.

The next question is, the Cepheid expert test is listed as both waived and moderate complexity. So this is very common for tests, to be listed as both high moderate and waived complexity, because they can be used in any of those settings. So if minimally trained operators-- such as those in a waived environment-- are able to operate a simple test, it's assumed that the more highly trained operators in a moderate or high complexity laboratory can also operate that test. So there is nothing to prevent a CLIA lab-- a CLIA high complexity lab-- from using a test that is also able to be used in a waived setting. Additionally, I believe with the Cepheid test they have two separate kits with two sets of instructions for the different settings.

Resources:

CDC Waived Tests webpage

CMS Clinical Laboratory Improvement Amendments (CLIA) webpage

Next question. Are there any saliva tests available as waived or moderate complexity for COVID only? No, at this time, all saliva COVID-19 tests are high complexity.

Regarding antibody testing, when is the rapid finger stick serology test for COVID-19 antibody IgG and IgM testing preferred? At this time there's only one serology test that is EUA authorized for a point-of-care use. And health care providers may want to quickly test for antibodies without the need to collect a venipuncture sample and send it out to a central lab, and in that case, the finger stick-- rapid finger stick test would be an appropriate use.

Let's see. With the new guidance on SARS-CoV-2 LDTs, can a lab take an FDA EUA test and lab-validate specimen stability to be greater than that stated in the package insert? So in order to perform a test under its EUA, it generally should be performed according to the authorized instructions for use. And that would include specimens stability. The use of increased specimen stability would be outside the scope of the EUA, and not authorized under the EUA.

As we noted in the guidance document, the "Policy for Coronavirus Disease-2019 Tests," the FDA has indicated that we generally do not expect EUA submissions for certain validated modifications to a previously authorized test. So such modifications would not be considered to be FDA-authorized, and should not be represented as such. And regarding marketing an LDT without an EUA, we would refer to the HHS statement on that topic.

Next question is why would LDTs for SARS-CoV-2 NAT tests on nasal determinate or saliva do not require FDA EUA review, whereas the same LDTs for the same specimens self-collected at home and mailed back to a certified labs do require submission to FDA EUA review? So generally, FDA does expect tests for home collection to receive an authorized EUA specifying at-home self-collection prior to marketing.

Home collection, even when it's observed over telemedicine, raises several issues of importance-- including whether the lay user can safely improperly collect the specimen, whether the components of the specimen transport media are safe for use in the home environment, proper shipment and adequate stability of the specimen given the time between collection and testing, and the potential impact of shipping conditions. There is additional information on that topic in our FAQ titled "Can I offer my test for self collection of a specimen at home and shipping to a laboratory for testing?"

Next question is does contamination of the nasal specimen with blood or snot contribute to false positives? It could, because that sort of error would be certain-- it could, but that sort of error would be covered by the interference testing that we look at for an assay. So the EUA templates that we've put out included our recommendations for that sort of testing, to determine whether those substances would interfere with the test.

Do we recommend confirming positives for asymptomatic and symptomatic? Each test includes in the authorization whether the results are considered presumptive. So for some tests, results from asymptomatic individuals are considered presumptively negative, and I believe that is also the case for some tests with positives. They may have presumptive positive included in the authorization. So the specific instructions for use should be consulted for each test.

Let's see. With many sports teams using tests for asymptomatic individuals, and false positives being reported on, it makes laboratory tests we're doing in labs be questioned on their validity. Do you have any suggestions on how to handle this question? So we also are hearing concern about false positives, and we're working on getting some additional information out about that. We generally discuss the fact that positive predictive value does vary with the disease prevalence when interpreting results. So as the disease prevalence decreases, the percent of tests that are false positives would be expected to increase.

We received a question asking, can you give a brief synopsis on the FDA guidance issued today? Unfortunately, I'm not completely positive on what guidance that was referring to. But since it was likely last Monday, I think it was probably referring to the antigen-- the update to the antigen EUA template that was issued that day. So that-- the EU templates all provide our current recommendations regarding data and information and that should be submitted to the FDA in support of an EUA request. So the antigen one is specific to antigen testing, and the update from last week added recommendations regarding studies to support claims for asymptomatic screening and multiplexed antigen tests.

Next question is, if FDA is no longer reviewing LDTs submitted for both serological and molecular COVID-19 testing performed in CLIA-supervised laboratories, does this apply to LDTs performed on at-home self-collected dried blood spots, or serology or saliva or nasal swabs specimens from ocular? If EUA submission is still required for early testing these latter specimen types, what is the rationale for such a requirement? So I already discussed a little bit the home collection, and that we do expect an EUA for tests for home collection. I do also want to point out specifically for dried blood spots and saliva, that it's also important for tests that are not done with home collection but are done at a traditional health care collection site-- we do expect LDTs to use legally marketed collection devices. So tests that are using unauthorized collection devices would be expected to come in for review in order for the collection device to be legally marketed, or the collection device to come in on its own-- such as the-- we have authorized, at this point, a few saliva collection devices.

And that feeds into the next question, which is, is there a standardized saliva collection method recommended? And as I said, collection should be done using a legally marketed collection device, and we've issued three authorizations for saliva collection devices. Those can be found on the EUA web page.

And the last question that I have here is whether there is a standardized definition or description for who can observe a self collection. And well, there's is not a formal definition. We do expect that to be done by a trained health care professional. And as I mentioned before,

home collection we consider separately. And from an FDA perspective, a health care provider watching a collection by way of telemedicine may address the issue of proper specimen collection, but it doesn't address the other issues that we have with home collections-- such as specimen stability and shipping conditions-- which would still be of concern.

And that is all the questions that I have. Jasmine, are there others that have come in? Or I think we may be running short on time, we can maybe--

JASMINE CHAITRAM: We did get a few more that came into the Q&A. I was just going to check if Sara Brenner also had an update, or should I just go to questions?

SARA BRENNER: Jasmine, you can go ahead and go to the questions. Thanks.

JASMINE CHAITRAM: OK, sounds good.

All right the first one is, what if the home collection kit has its own EUA approval? Does the lab still need to submit a separate EUA application? So the home collection kit has its own EUA-- which I don't know that we have that independently, but the question is does the lab need to submit a separate EUA-- I guess to do a test?

TOBY LOWE: Right. So right now all of the home collection kits that we have authorized are specific to tests that are authorized for use with those collection devices. So we would expect tests for use of home collection specimens to come in at this point.

JASMINE CHAITRAM: OK. Sorry, I've got one more. I understand that FDA no longer reviews EUA applications for SARS-CoV-2 molecular tests developed and performed in a single high complexity laboratory. If we implement an EUA approved, unobserved specimen collection kit in conjunction with our COVID LDT, is it sufficient to perform an appropriate internal validation, or a formal application of EUA review is needed?

TOBY LOWE: As long as it's not for home collection and it is using an authorized collection device, we would not expect to see an EUA request for that.

JASMINE CHAITRAM: Thanks, Toby. I've got one more for you. I'm just trying to remember where it went.

TOBY LOWE: Sure. I'm seeing, if I'm looking at the right place, I'm seeing a question asking about an update on the BD MAX SARS-CoV-2 reagents, and--

JASMINE CHAITRAM: Yeah, go ahead and answer that one, and then I'll ask you one more.

TOBY LOWE: Sure. I believe that based-- that that assay does still have presumptive positive limitations in their labeling. So the labeling that is up on our website is the current labeling for that.

JASMINE CHAITRAM: Thank you. And so the next question I had was, understanding the root cause of false positives can be important? Some causes of false positives are amenable to mitigation-- for instance, operator error or instrument overheating. Others-- such as a cross reaction of antibodies with seasonal coronaviruses-- might not be amenable to mitigation. Is FDA gathering information on causes of false positive antigen tests?

TOBY LOWE: That's an interesting question. So we are working on getting additional information out about false positives. If there-- if you have information that you think would be useful for us to know about causes of false positives, we would be interested in having that, and would ask that you send it to the email address that's shown on the screen right now.

SARA BRENNER: Jasmine, this is Sara Brenner, also from FDA. But in [INAUDIBLE- voice cut out] Toby's answer for FDA, we're very interested in that. I'll add that, from an inter-agency perspective at HHS and looking at diagnostic data, evaluating real-world test performance is something that is a top priority as we sift through the reams and reams of diagnostic data that are being reported, including many of the data elements that were required under CARES. So there's a whole slew of them that we're looking at, in terms of collecting both reported evidence and also what we call real-world evidence-- or real-world data-- to better understand where specific IBD platform. So that's right down to the very specific test being used, where they're being used most appropriately, for what populations, and under what circumstances.

There are other data elements also being reported having specifically to do with each diagnostic device and, for example, the dates where specimens are collected and then analyzed, the type of specimen, and the complexity of the lab running the tests. So just an aside, note that there are a lot of ways that we're trying to better understand how tests are really performing in the field after they've been authorized-- so their post-market use, in other words.

JASMINE CHAITRAM: Thanks, Sara. And thanks, Toby, as well. It's really nice to see your face after working together for so many months. Putting the name and the voice with the face has been great. So I appreciate your time on the call today. Thanks Sara, also, for being here.

We are-- we just have a couple more minutes, so I'm going to wrap it up by providing a couple of links to our CDC social media websites, where we post information about new guidance, and also remind everyone that our next call will be on Monday, November 16. If you're not already receiving messages from CDC by email through the LOCS-- the Laboratory Outreach Communication System-- please send us an email to LOCS@cdc.gov, and we can get you on our distribution list. And as always, thanks to everybody that's out there fighting the fight every day and trying to help with this COVID response. We appreciate everything that you're doing, and we hope that you're staying safe.

Thank you, and we'll talk to you again in two weeks.