

Virtual Town Hall Number #77
January 26, 2022

Joseph Tartal: So hello, and thank you for joining us today. I'm Joseph Tartal, Deputy Director in the Division of Industry and Consumer Education in CDRH's Office of Communication Education, and I'll be moderating today's program. Welcome to Virtual IVD Town Hall Number 77 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in response to COVID-19.

Today's presentation and transcript will be made available at CDRH Learn under the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. Please note we are working to post the recording and transcript from the last Town Hall that was held on January 12. We hope to post it soon. The next scheduled IVD Town Hall will take place Wednesday, February 9, 2022.

Our panelists for today's program are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health, or OIR, in CDRH's Office of Product Evaluation and Quality; Toby Lowe, Associate Director for Regulatory Programs in OIR; and Dr. Kristian Roth, also in OIR as the Deputy Director of the Division of Microbiological Devices.

With that, we will begin with open remarks from our panelists, and then we'll answer your previously emailed questions about COVID test development and validation. Please note, we received some questions that are too detailed or test case specific that we will not address on the call. For those questions, we'll try to send a response in writing within a few days.

If you have submitted a question and do not hear it addressed, please look for the written response. If you do not receive one within a few days, please feel free to reach back out to CDRH-EUA-Templates@fda.hhs.gov for an update. Last, we'll open up the live lines for your questions. So with that, I will now hand over the program to Toby for opening remarks. Welcome, Toby.

Toby Lowe: Thanks, Joe. Thanks, everyone, for joining us again this week. So, I do have a handful of updates, and then we'll get into the questions. So, following the last Town Hall, we became aware that there was some confusion over the discussion about distributors.

Generally, we recommend that all EUA holders refer to their conditions of authorization in their letter of authorization to determine what needs to be sent to FDA and in which cases they need concurrence from FDA prior to implementation. In general, the conditions of authorization typically state that an EUA holder must tell the FDA of any new distributors and must have concurrence from FDA prior to implementation of any updated labeling, including any new brand names.

So, the concurrence is generally only if there is updated labeling. If you are adding a new distributor without changing any labeling, we will generally acknowledge receipt, but you do not need to wait for concurrence. And that is, again, dependent on what is in your letter of authorization, but that is the typical situation for most EUAs.

And then we do also continue to receive questions about plans for submission of a 510(k) for molecular SARS-CoV-2 tests. We've generally recommended that developers submit a presubmission to discuss their approach, and we've stated that previously on this call many times. At this point, we are able to provide feedback more rapidly.

So we welcome any developers that are considering a 510(k) for a molecular SARS-CoV-2 test to send an email to the EUA mailbox requesting feedback regarding submission of a 510(k). And for those developers that have already submitted a presubmission, you don't need to do anything differently. We will get that feedback to you through your presubmission.

A couple more updates on previous actions. On the 19th, just last week, we issued an EUA for the MaximBio ClearDetect COVID-19 Antigen Home Test. That's another over-the-counter rapid test that went through the ITAP program.

And then on Friday of last week, we also updated the IVD EUA Molecular and Antigen web pages to add information about whether each authorized assay is a single or multiple target test. And this is intended to better inform potential users which tests are more susceptible to changes in performance due to viral mutations.

We also added a new FAQ to the Test FAQ page regarding the inclusion of multiple targets to protect against performance impacts from future mutations. And then on Saturday the 22nd, we added an FAQ and put out some social media regarding the use of tests that are shipped and left outside in freezing temperatures.

And the last update, last month in December, FDA issued a draft guidance titled "The Transition Plan for Medical Devices Issued EUAs During the COVID-19 Public Health Emergency." That is a draft guidance that was issued for comment, not for implementation. And we have received some questions regarding how specific situations would be handled under that guidance.

Since that guidance has been issued in draft for comment and not for implementation, if there are points about the guidance that are unclear, we recommend that you submit a comment to the docket indicating areas that could benefit from added clarity.

And if you have a question about how to manage your current plans for moving forward now with your emergency use test or with a 510(k), we recommend that you send an email to the EUA Templates mailbox with sufficient details so that we can provide appropriate feedback for your particular situation. And with that, we can move into the questions that we received by email.

Joseph Tartal: Thank you, Toby. And thank you for sending your questions by email. And I'll get started with the first question for Toby. What is required for a telehealth provider for home rapid tests?

Toby Lowe: Sure, yeah, so tests that use a telehealth proctor are validated with the proctor as part of the test and are authorized as such based on that performance data. So a developer that's looking to include telehealth proctor as part of their test should submit an EUA request demonstrating appropriate performance of the test with proctoring. This allows the FDA to ensure that the tests are able to be accurately performed via telehealth and accurately read via telehealth.

Joseph Tartal: OK, thank you for that answer. So our next question is, how should test developers address the omicron variant in clinical studies for new antigen tests?

Toby Lowe: Now, any new EUA requests should include clinical data from patients infected with omicron to ensure that the test performs well with this variant. As discussed in the policy for evaluating

the impact of viral mutations on COVID-19 tests, the FDA considers performance across all known variants as well as—

Joseph Tartal: So I hear-- I mean, I think I see that Toby's talking, but I do not hear anything.

Toby Lowe: Are you able to hear me, Joe?

Kristian Roth: I hear you, Toby.

Toby Lowe: OK. All right, so I'll continue with that one. We do consider performance across all known variants as well as the developer's plan for ongoing monitoring of new and emerging variants. As we saw with omicron, several tests were impacted by the mutations in the omicron, so this is an important review consideration. And we would ask that you discuss with your FDA reviewer the expectations in that regard.

Joseph Tartal: OK, thank you. And now we'll move on to our third question. And I believe Tim will answer this. Will FDA consider throat swabs for at-home COVID-19 diagnostic tests?

Timothy Stenzel: Thank you, Joe. Short answer is yes, but let me go into some detail. As stated in the previous Town Hall meeting, the CDC does recommend that throat swabs be collected only by trained health care providers. While the FDA is open to the sample type for rapid tests with data demonstrating that the safety concerns have been addressed, there has been some new evidence published.

That's a UCSF paper preprint that is on the slide deck and can be referred to. I will briefly outline the key findings from that paper. They examined the use of an oral cheek swab and what they call a throat swab, which I believe is an oropharyngeal swab, for use with one of the EUA-authorized rapid antigen tests.

And they compared it to nasal swab and did have a PCR comparator as well. They found that either the cheek swab or the oropharyngeal swab alone had sensitivities that were considerably below the nasal swab alone.

And when they obtained a combo nasal and oropharyngeal swab, the slight sensitivity improvement was, in their opinion, did not benefit testing enough considering the risks of oropharyngeal swabs, both to health care workers who might be performing it and to the user.

There is frequently gagging and even throwing up. This can potentially spread disease within the health care environment, and obviously, would also be a problem at home in obtaining an adequate sample.

Also, omicron may be unique in its tissue where it replicates more readily versus the other viral variants. For example, the previously mentioned South African paper showed for delta that a nasal swab was better than saliva in their hand.

So it would be a lot of work to go through and validate something that may not be the best thing for patients or for care. And then you have the next variant come along and it returns it to being the nasal swab being the best. So I think that pretty much covers our thoughts on throat swabbing, so thank you.

Joseph Tartal: Thank you, Tim. Let's go on to our next question. Regarding FDA's condition of emergency use authorization limiting the emergency use of tests to authorized laboratories, does the manufacturer have a duty to confirm a laboratory's CLIA registration status and type prior to shipment and maintain a record of this review, or does the responsibility fall with the laboratory to only use if qualified to do so?

Toby Lowe: So it is the responsibility of the EUA holder or the authorized test distributor through the process of inventory control to adequately maintain records of authorized laboratories to which they distribute the test and the number of tests they distribute. So the EUA holder should be confirming that they are distributing only to appropriate laboratories.

Joseph Tartal: OK, thank you, Toby. And our next question, is it acceptable to use the candidate test to screen negative clinical matrix used for analytical validation instead of using an authorized or cleared asset?

Toby Lowe: Yes, it is acceptable to use the candidate test to confirm negative clinical matrix that will be used for analytical validation studies.

Joseph Tartal: Thank you for that answer. And our next question, since IDT is no longer selling CDC-qualified lots of reagents, how should labs using a modified version of the CDC assay handle the use of the RUO, Research Use Only reagents from IDT?

Toby Lowe: So CDC, as we've discussed here before, has stopped qualifying lots for IDT to sell. They have stopped supporting their SARS-CoV-2-only assay. But they have also provided recommendations for laboratories that are using that CDC-- the original SARS-CoV-2 CDC assay to transition to another FDA authorized COVID-19 test.

Laboratories that intend to continue performing testing using the RUO reagents, the non-qualified lots of reagents from IDT, should include qualification procedures for qualifying each lot of reagents that they purchase. CDC has provided their qualification procedures to FDA, and we're able to provide those to laboratories that need them. Excuse me. If you do need them, you can email the EUA mailbox and ask for those.

Generally, since the CDC test is an authorized test, they still hold an EUA. Even though it is not being distributed any longer, labs may offer a modified version of the test under the modification policy that's included in the November 15 guidance. And so we do recommend that laboratories should consider the policies discussed in that November 15 version of the guidance the policy for coronavirus disease 2019 tests to determine whether they need to submit a new EUA request to the FDA.

Joseph Tartal: Thank you, Toby, for clarifying that. And we'll go on to our next question. For an over-the-counter antigen all-comers clinical study, is it acceptable to exclude individuals for symptom onset greater than a certain number of days to exclude individuals with lingering symptoms?

Toby Lowe: So if you're performing an all-comers study including symptomatic and asymptomatic individuals, you should not exclude anyone based on their symptoms. Instead, you should record this information, including for symptomatic individuals, the days since symptom onset. And you should also record any known exposures.

Samples that are outside of the specified date range that you're requesting for your intended use should not be included in your primary determination of the agreement between your device and the comparator test. For example, if you're proposing an intended use for symptomatic individuals seven days post-symptom onset, then we would want to see performance data to support that intended use, and other data should be excluded from your primary determination of NPA and CPA.

Joseph Tartal: Thank you for that answer, and going on to our next question. There is emerging evidence that rapid antigen tests may be less sensitive in detecting the omicron variant of SARS-CoV-2 than earlier variants. Is FDA considering changing the recommendation for 80% PPA with 70% lower bound of the 95% confidence interval for rapid antigen test to recognize this challenge in the omicron variant detection?

Toby Lowe: FDA is not anticipating modifying the performance recommendations for antigen tests. Particularly as the use of rapid antigen tests increases, it's important that these tests are able to detect known variants, including omicron. Antigen tests are already labeled with a presumptive negative claim given the lower PPA than most molecular tests, and we do not anticipate reducing that performance recommendation any further.

As additional information becomes available about the impact of omicron or future variants on diagnostic tests, we will continue to update the website with this information. And we do have a specific SARS-CoV-2 viral mutations impact on COVID-19 tests website that we update regularly.

Joseph Tartal: OK, thank you for that information. And we're getting now to our last email question that came in. Please keep those coming for the next and future town halls. So the last question is, is FDA still considering emergency use authorizations for multi-analyte over-the-counter tests?

Toby Lowe: Yes, the FDA continues to recommend that developers interested in pursuing an EUA for an over-the-counter multi-analyte test to submit a pre-EUA to further discuss your proposal.

Joseph Tartal: OK, thank you very much, Toby. And with that, we are now going to transition to the live questions. So now let's take your live questions. To ask a live question, please select the Raise Hand icon at the bottom of your screen. When you are called on, please identify yourself and ask your question promptly.

Also, please note we are not able to discuss specific submissions under review. Again, for those type of questions, please email the EUA Templates mailbox. So with that, we're going to get to our first question. MHK, I'm unmuting you. Please unmute yourself and ask your question.

MHK: Hi. Yes, good afternoon. Question is for the-- is there a cutoff for the CT values for the data that we present? And also, you mentioned just now that we need omicron data. Would the patient sample need to be sequenced to confirm that, or how would you verify that that strain is present? Thank you.

Timothy Stenzel: Yeah, yeah, could you clarify what kind of test you're developing?

MHK: It's an antigen SARS-CoV-2 test.

Timothy Stenzel: OK. Yeah, so we want CT results for all of your clinical samples. See our antigen templates on the FDA website. And we want to see all the data. We don't want any data excluded. And

we want to see a certain number of low positives, which are defined in the template about what low positives are. And we use CTs to do that. And we want your comparator molecular test to be an acceptable high sensitivity one, so do check with the FDA prior to using that test.

I want to pause here. I hope I answered all the questions, but I may have missed one subpart.

MHK: Yeah, I think that's answered that one. And I think the other one was how do we show that we have omicron data? Do we need to sequence every sample?

Timothy Stenzel: Eventually we'll want-- Yeah, eventually we want sequence confirmation, but it depends on the situation. So if you've not done your clinical study yet, yes, go ahead and sequence your clinical study samples. Omicron, last time I looked, was about 99% or greater in the US. So any study that's done right now is going to most likely be omicron, and the sequencing will confirm it. Just make sure the sequencing method has been validated in some way.

If somebody is already in with a submission and we're now asking for omicron information, they should work that out with their lead reviewer about the number of samples we want to see because they may have already completed a study with delta and the other information we need about those samples prior to making an authorization decision.

MHK: OK, thank you very much.

Timothy Stenzel: OK.

Joseph Tartal: So we'll go to our next question. I'm going to unmute you Wenli. So please, Wenli, unmute yourself and ask your question.

Wenli: Hi, thank you very much. And so just to follow up with the last question, right now you said that everywhere is more than 99% is omicron. If we just start a clinical trial, we don't need to confirm any sequence for omicron, right?

Timothy Stenzel: Yes, please do. If you haven't started your trial, clinical study yet, please go ahead and plan to do the sequence analysis. There is delta circulating in some areas and some pockets in the United States, and you just may have hit a pocket that has more delta than others. So it's important for us to know that it's omicron.

Wenli: So basically, for all the samples, you need the sequencing confirmation that—

Timothy Stenzel: All the positive samples.

Wenli: OK, got it. Thank you.

Joseph Tartal: Thank you. We're going to go to our next stakeholder, Rahul. I'm opening up your mic. Please unmute yourself and ask your question.

Rahul Sharma: OK, so we are-- we've got a very small-- starting a small lab, RT-PCR based. Do we have to submit for EUA or we can do the artificial as LDT?

Timothy Stenzel: Well, see the November 15, 2021 guidance and see how it will apply to you. There are hundreds of molecular test opportunities, and there is no shortage of all molecular kits that are available for use in a lab. And so we do encourage those. If someone wants to pursue an LDT, look to the guidance.

But now, the FDA is saying that a submission is needed if it hasn't already been made under the guidance. Toby, anything else to add?

Toby Lowe: Yeah, I would just add since you specified that you're starting a new lab, that leads me to believe that you're not-- haven't begun testing. So for any new tests, including LDTs, and this is spelled out in the guidance that Tim is referencing, and we do expect an authorization, fully authorized and not just submitted an EUA request prior to testing.

Rahul Sharma: Even if it's not testing that is as in guidelines, it says to scale up the testing? We're only testing 100 samples a day?

Timothy Stenzel: We want to make sure that those 100 samples a day are accurately tested.OK.

Toby Lowe: Yep, so taking a look at the guidance, and it does specify that we expect all new tests to be authorized.

Timothy Stenzel: Yes, and so if you're only going to do 100 tests a day, it's unlikely to meet our volume expectations for review, and therefore, an EUA would not-- that your submission wouldn't be reviewed due to low volume testing. This doesn't apply to any tests that were already validated by November 15, 2021.

We are not applying any volume metrics to that. It was on the market. We wanted to facilitate it staying on the market. But any new tests that come in after the guidance will need to-- of any type, whether it's manufactured kits or LDTs, will need to meet the volume minimums in order to substantially increase the amount of testing that's performed in the United States. Those are the guidelines. That's the policy.

Rahul Sharma: So just saying that we will not review the test that does not meet the volume criteria, but we cannot offer that as a LDT, so that means--

Timothy Stenzel: We will not review and, no, you cannot offer, as Toby said, without in an EUA authorization.

Rahul Sharma: So the labs and the new labs cannot offer low volume testing. That's what--

Timothy Stenzel: Yes, they can. They can offer. They can absolutely offer low volume testing. They just need to go ahead and purchase one of the manufactured kits that's been authorized.

Rahul Sharma: OK, but not as a LDT.

Timothy Stenzel: Correct.

Rahul Sharma: OK, thank you so much.

Joseph Tartal: OK, thank you. And our next question is from Vitali. I'm unmuting you right now. Please unmute yourself and ask your question.

Vitali Karaliou: Hi, guys. Thank you for these town halls, very helpful. So I represent a small biotech company, ArtBioTech. So we are scheduling a clinical trial for all molecular PCR express tests. And it looks like we meet guidelines November 15, 2021 for the EUA, so we'll definitely do pre-EUA to discuss details.

So just a quick question before that. We plan to use specimen leftovers to speed up the study to minimize risk and lessen this exposure to the staff. And the question is, would this data based on the leftover specimens be potentially transferable into 510(k)? And using these leftover specimens just follow up, do you have any comments on the inclusion of asymptomatic patient populations into this kind of study? Thank you.

Timothy Stenzel: So can you-- are you a kit manufacturer?

Vitali Karaliou: Kit manufacturer.

Timothy Stenzel: And what's the type of kit that you are going to produce?

Vitali Karaliou: It's molecular PCR express test. We looks like we meet guidelines. We have high throughput, short particle—

Timothy Stenzel: Yeah, if you want to include asymptomatics, check the current templates on the FDA website. There are a number of different possibilities that you can propose. But we would want to see the actual data in asymptomatic individuals in order to make an authorization for asymptomatic testing. Toby, that's correct? Kris, that's correct, right?

Vitali Karaliou: So specimen leftovers are probably not the way to go with asymptomatic, but with symptomatic should be fine, right?

Timothy Stenzel: Well, symptomatic's very straightforward. You test symptomatics. You probably want to limit how many days they've been symptomatic, and you don't want to probably go beyond 14 days. And you can look at other molecular authorizations. Toby, Kris, any additional thoughts? I think that means we're good.

Vitali Karaliou: OK, thank you.

Kristian Roth: I think I'd look at the template for asymptomatics because there's couple of options there. And you were talking about leftover samples, then it depends on how they're collected. So all that is outlined in the molecular-- sorry, molecular template. Excuse me.

Joseph Tartal: OK, sounds good. So let's go on to our next question. Jiayan Liu, I'm going to unmute you. Please unmute yourself and ask your question.

Jiayan Liu: Thank you. This is another question regarding the omicron variant. We are developing a new nucleocapsid test, and the clinical studies are ongoing. Before this, we have an in silico analysis showing

that the new variant has no impact in our test. So the question is, is this in silico analysis is sufficient, or are we required to include the omicron patients still?

Timothy Stenzel: Yes, but thank you for that question and the opportunity to clarify. The actual patient sample testing with omicron is only going to be needed for antigen tests. The molecular tests can be used. The in silico analysis can be used for the molecular test. If the FDA review team has any concern about any variants and mutations in the in silico analysis, they will discuss that directly with the test developer. So yeah, my remarks regarding omicron and the need to see clinical samples is only for antigen tests.

Jiayan Liu: That sounds good. Thank you.

Joseph Tartal: All right. Thanks for that clarification--

Timothy Stenzel: And the same-- yep, and the same thing goes for sequencing of samples. For the molecular tests, we don't need to know if they're Omicron or not unless there is some issue we need to look into. Thanks.

Joseph Tartal: OK, our next question is from Ho-Jun. Ho-Jun, I'm unmuting you. Please unmute yourself and ask your question.

Ho-Jun Suk: Thank you. My name is Ho-Jun and I'm from PX Lab. And I had an-- we're developing a molecular point of care diagnostic test for COVID. And I had a quick question on the environment for the region stability, specifically on open kit shipping stability requirement for this submission.

The most recent molecular template talks about the summer and winter storage conditions or temperature conditions to test for, but it doesn't necessarily mention any international standards for shipping/distribution simulation. I was wondering if the FDA had any specific guidance/recommendation as to which similar distribution simulation standards we should follow for this shipping stability study? Thank you.

Timothy Stenzel: Yes, if it's not in the templates, we can provide that. Kris, I'll turn it over to you as well here. You can probably just email the Templates email box and get a pretty quick response, or put it in a pre-EUA, if you're putting in a pre-EUA, though I don't necessarily recommend a pre-EUA for this. But Kris, do you have some more helpful comments than mine perhaps?

Kristian Roth: No, I think that's the best route to go. We're open to using any ASTM standard that may be widely applicable. And so, if you have an idea of what you want to follow or what you think is appropriate, then you can go ahead and propose that to us as well.

Great, and just one quick follow-up to this question. Is it necessary to have this shipping stability data as part of our full EUA submission, or could this be something that could be provided after or during the process?

Timothy Stenzel: We would recommend that you begin it, and then, if it's not completed by the time it's time to make a review decision, have a conversation with the team. There could be certain things that can impact that in fact. So for example, if a molecular kit is shipped on dry ice and it's required to be

received on dry ice, that would be a potential mitigation for heating and cooling during shipping. So Kris, anything else to add?

Kristian Roth: No, I think at least we'd want a plan and so we can discuss that plan in the context of your EUA.

Ho-Jun Suk: Amazing, thank you so much.

Joseph Tartal: OK, our next question is from Josh. I'm unmuting you now. Please unmute yourself and ask your question.

Josh Perfetto: Hi, thank you. This is Josh Perfetto from Chai Bio. We have a molecular test that's on your current notification list, and we've been working with CLIA Labs throughout the pandemic to get them up and running with this. Under CMS, these labs had to perform an additional validation because the test is not FDA authorized, which as I understand it, is the same sort of validation that they would have to do to make for their own LDTs of things like LoD and background and all that stuff.

So my question is with the recent change in the guidance, whether new high complexity CLIA labs that are performing this validation to run our kit, does that basically make it be considered an LDT under FDA regulation and therefore, that they would have to submit and await approval of their EUA to run that test? Or can it continue as before the change? Thanks.

Timothy Stenzel: That's an interesting question. I don't think so, but let us double check and we'll respond. You can send that question directly to the Templates email address and ask for Tim and Toby to be copied. And we'll try to get you a response. Oh, I think Toby can answer this. Go ahead, Toby.

Toby Lowe: Yeah, so if I understand your question correctly, you are distributing a validated test kit under the notification policy. Is that right?

Josh Perfetto: Yeah, that's correct.

Toby Lowe: And you have an EUA currently under review that has not been-- a decision has not been made on that EUA request. Is that right?

Josh Perfetto: Yeah, correct.

Toby Lowe: OK, then under the November 15 policy, as long as you have-- as long as your submission was either after, I think it was February of 2021 or before that, if you've let us know that you want us to continue to review so your submission is actively under review, then you can continue to distribute your test to high complexity CLIA certified labs-- excuse me.

And they can continue to perform it as a notified test kit under that continued distribution during FDA review policy. That's laid out in the November 15 guidance. We do not expect those labs that are using your test kit to submit anything to FDA.

Josh Perfetto: OK, great. That's what I want to know. Thanks for the information.

Toby Lowe: Yep.

Joseph Tartal: OK, thank you for that answer, Toby.

Toby Lowe: And just to-- sorry, just to add to that, I was just confirming. We do have a question on our FAQ page. It's on the page that includes the notification list. We do have a question that addresses that, as well, if you want something in writing to share with the lab.

Joseph Tartal: Thank you, Toby. And with that, we'll get to our next question. Tianyang, I'm going to unmute you. Please unmute yourself and ask your question.

Tianyang Liu: Hi. My question is we got to know that some over-the-counter holders that, for example, ACON has some labeling issue before or should-- is it legally, I mean, the FDA issue has already been resolved and should it be-- could we buy it in the market right now?

Timothy Stenzel: So any EUA authorized test can be purchased. If you have any question about the authenticity of any test, there are situations out there that all labs should be cautious about. For example, there are many tests that have CE marked versions that have not been reviewed by the FDA. And it's important that users in the United States only get the EUA authorized version.

If you have any questions, you can always contact each individual manufacturer and make sure that the tests that you're about to purchase are legitimate, bona fide, and EUA authorized versions of their tests.

Tianyang Liu: OK, thank you very much.

Joseph Tartal: All right, thank you. For our next question, Ela, I'm going to unmute. Please unmute yourself and ask your question.

Ela Heussen: Hi, this is Ela Heussen from Abreos Biosciences. I'm wondering what the review times for pre-EUAs and EUAs antigen tests are these days and when one should expect to hear back?

Timothy Stenzel: So I would recommend restricting pre-EUAs to only questions that aren't covered in the template. Things are pretty clear. And then we can get back to you more quickly. And we do recommend following the FDA recommendations on things because there are a lot of interested parties in this.

Once an antigen test is received, it's quickly reviewed for completeness. If it's not complete, we'll get back to you in a few days letting you know it's not complete. But once it's accepted for review, this is the highest priority area within the FDA. And I would personally routinely monitor turnaround times on this and speak to the antigen team to make sure that we move these things along quickly.

But unfortunately, we can't promise any defined turnaround time. We are seeing a lot of submissions through the ITAP program and through the RADx program. And so, in addition to other submissions, we are continuing to have a high volume of antigen test submissions.

Ela Heussen: Thank you.

Joseph Tartal: OK, thank you. And please, if you have any questions, select the Raise Hand icon at the bottom of your screen. And when you're called on, we'll unmute you and then you can unmute yourself

to ask more questions. I saw a hand pop up and then disappear again. Please, we still have a few more minutes. If you have time, ask your question.

Timothy Stenzel: Looks like we have some questions.

Joseph Tartal: See some other ones popping up. Wenli, I'm unmuting you. Please unmute yourself and ask your question.

Wenli: I thank you so much. That's just nobody's here now, just have my second question. Thank you.

So on the question about we talked about earlier on the qualified CDC primer and probes, what do you mean by qualified? Is that because the CDC only for the multiplex assay, they only send it up the primers and probes to the public laboratories, as far as I know. Does that mean there's no way for private laboratories to get a qualified primer and probes? And I think that's my question.

Timothy Stenzel: It used to be--

Toby Lowe: Yeah.

Timothy Stenzel: Go ahead, Toby.

Toby Lowe: Yeah, so the CDC announced that they were no longer supporting their SARS-CoV-2 single analyte test. They announced this last summer. While they were supporting the test, they were qualifying lots of reagents that were sold by IDT, which is a reagent manufacturer. And so, private labs could purchase those qualified lots of reagents from IDT and been able to offer or to perform the CDC assay as authorized.

Since CDC is no longer supporting that assay, they are no longer qualifying lots that are distributed by IDT. But IDT is continuing to distribute unqualified lots or RUO lots. And so in that situation, a laboratory would have to qualify those lots themselves.

Timothy Stenzel: And I would just add that in the early days, Biosearch also had lots that were qualified by the CDC, but they have also ceased distributing those qualified lots.

Wenli: So basically, it's qualified lots and the primers. And they were distributing, and they may stop. So if we have the qualified primer probes, either for a single one or for multiplex ones, then they can-- can the assays still be used as a comparator for the antigen tests?

Timothy Stenzel: Yes, if you have-- if you have purchased lots that were qualified by either of the two sources while the CDC was still qualifying them. Those were all sold, well, I think the last sales were on and around or before September of 2021. Just check with whoever you purchase them from, IDT or Biosearch, and determine if your lots were qualified by the CDC or not.

The CDC EUA remains in force, and those tests can continue to be used, although the CDC has recommended that labs move away from that because those qualified lots are going on-- those qualified tests are going away. Toby, is that good?

Toby Lowe: Yeah, absolutely. And just to add that the CDC is still supporting the multi-analyte test so there are still qualified lots for that test being sold.

Timothy Stenzel: But I don't believe they're being sold independently. I could be wrong. I don't think the CDC was ever qualifying those tests to be made by other manufacturers, those multi-analyte meaning flu and SARS-CoV-2 are only being distributed to public health labs.

Wenli: Correct.

Toby Lowe: Thanks for clarifying that. Sorry for that confusion.

Timothy Stenzel: Well, we have a lot of questions here. So let's go ahead and move on. Thank you.

Joseph Tartal: So I'm going to unmute you, Najwa. Unmute yourself and ask your question please.

Najwa Lamnii: Hi, so we are a CLIA certified lab. And in addition to having our own LDT, we also use other EUA approved tests. So I was just wondering what is our responsibility when it comes to confirming that the EUA is still valid, that they're not revoked as a CLIA testing lab?

I know that if we were purchasing them for the first time, you mentioned we just have to confirm with the manufacturer. But do we have any specific requirements when it comes to confirming it while we have been using it?

Timothy Stenzel: So if you're buying a manufactured kit that is either that is EUA authorized, the FDA does not have any recommendations on what the lab would do. But I believe CLIA has some policies that need to be followed for that. Toby covered what labs might need to do if the test is notified and not yet in on the notification list, but not yet EUA authorized. Does that answer your question?

Najwa Lamnii: So once they are authorized, we should still make sure that they stay on the authorization? So if their EUA is revoked for some reason, we should be notified that or we should check it?

Toby Lowe: Yeah, so the EUAs are not revoked often. If an EUA is revoked "for cause," quote unquote, because an issue is discovered, that would be-- there would be an announcement about that. And we would also likely ask the company to perform a recall, so to notify all of their customers.

Other revocations are typically for when the manufacturer has decided that they no longer want to support their test. And so they ask us to revoke it. Those are all posted on our website. So if you look on our EUA website, as long as the test that you're using is there, there's nothing that you should be concerned about. And if anything is revoked that's in active distribution, generally an announcement will be sent by the company to their customers.

Najwa Lamnii: Thank you.

Joseph Tartal: Our next question is from Geetha. Geetha, I'm unmuting you. Please unmute yourself and ask your question.

Geetha Rao: Thank you. My question is something that I think, Toby, you've already clarified in a slightly different context. So I thought I'd take the opportunity to confirm my understanding. So the situation is I'm working with an LDT that had initially filed an EUA request that way back in 2020. The FDA had declined to review. We have subsequently filed a notification and received, I guess, a triage notice of some sort that the EUA was under review. The filing is under review.

I just want to clarify two things. First is even though the FDA website shows this LDT as not authorized, which is somewhat confusing to customers, it is OK to continue offering the test, because we have not yet received the EUA? It's under review.

Toby Lowe: Yeah, so just to clarify, the second EUA request you submitted after the November 15 guidance was issued?

Geetha Rao: That's correct. That's correct.

Toby Lowe: OK, then yes, under that policy, you can continue to offer the LDT unless and until we send you a notice saying that we've declined to review or declined to issue rather, and in which case, that letter would then spell out what we expect you to do.

Timothy Stenzel: Is your test on the website, on the FDA website, saying it was not authorized or—

Geetha Rao: It's under the LDT list. It's under the LDT.

Toby Lowe: It's under the notification list. The notification does specify that they are not authorized, just to be clear about the status of the submission.

Timothy Stenzel: Then unless it's under the umbrella policy of November 15, 2021, it is still not authorized. So that notification list is still correct. And there, as Toby said, there's no issues with you continuing to use that test while the FDA reviews. If we have any issues, we will reach back out. We hope those are few and far behind-- few and uncommon. But we will reach out. And all the while, we'll try to work with you to get that test back on to stay on the market. All right?

Geetha Rao: Great. Thank you. I have a really short follow up on that. And if the test is currently offered through the company's own CLIA certified lab, if the company wanted to create a second site that is CLIA certified with everything is internal. It's just a second site. Would that be OK with the current authorization or current non-authorization?

Timothy Stenzel: That would turn the test into probably not being an LDT. So I would submit that specific question into the Agency to our Templates email address so that we can make sure that we understand all the facts and can give you the right feedback on what to do in that situation.

Geetha Rao: Great. Thank you.

Joseph Tartal: OK, with that we're running short on time. We're going to go to our last question of the day. Karen, I'm opening up your mic. Please open up your mic and ask your question.

Karen S: Thank you. So I had a question pertaining to usability studies. I am conducting a series of usability studies for products that contain both paper-based instructional materials as well as app-based instructions and reporting capabilities. So the app itself is not needed for interpretation, but it can help.

So per the template, we are looking to include at least 30 participants in the study. Is it the expectation that there should be 30 participants for both the paper-based instructions and 30 for the app? Or can we use some sort of hybrid and maybe 30 paper-based participants and then maybe an additional 10 for the app? Thank you.

Timothy Stenzel: So yeah, and this is just the usability, but some of this would roll into the actual clinical study. The FDA doesn't assume somebody gets a kit, that where the instructions need to be provided, that are provided always in paper, that everybody will have access to the internet and access to an electronic form.

And so our primary focus is on the acceptability of the paper version. We're not opposed to extra training materials or the use of electronic instructions. As far as how to-- and I would hope that we wouldn't require you to do two studies or twice as much usability study, so I'm not sure if-- hopefully Kris is still on and/or Toby can respond about any more specificity to this. But Kris, you want to take that?

Kristian Roth: Yeah, unfortunately, I don't have an answer for you now. But I know we've addressed this in the past for other folks. And certainly, we're not going to duplicate 30 folks for both the paper and form based instructions. So I think if you can just email me that question. Or sorry, email the Templates inbox and have them CC me. I can get you that answer pretty quick.

But that would be ask for Kris Roth to be brought in, and he'll get you a quick answer.

Karen S: That's terrific. Thank you.

Toby Lowe: One thing that I just want to add. I think that I heard you say that the app is not needed for interpretation, but can help. I think Tim mentioned that this would also feed into your clinical study a bit. And so that is one consideration that we do want to see how the performance may be impacted with that step. So we would want that.

And again, if you send us in and copy Kris, we can make sure that we get you the right feedback there. But just wanted to point out that we would want to see how the different sets of instructions and especially with using an app for interpretation would impact performance or potentially impact performance.

Timothy Stenzel: Yeah, we would want to see the differences between paper and the app. And if the app is actually reading the test and independently interpreting it, then that's an entirely different situation.

Karen S: Yes. No, it's not reading it. But it can help in interpretation. It could walk you through that.

Timothy Stenzel: Right, right, so we would just want to know how the app differs-- in your email to Kris, how the app differs from the paper version in helping individuals do the test.

Karen S: Thank you very much.

Timothy Stenzel: Mm-hmm.

Joseph Tartal: Thank you. And thank you, Tim, Toby, and Kris. And thank you, everyone. We greatly appreciate your participation today for this great program. Today's program and transcript will be made available at CDRH Learn. Please visit CDRH Learn at www.fda.gov/training/CDRHLearn. You will find the recording and transcript in the subsection title Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series.

For additional questions about today's Town Hall and COVID-19 IVD topics in general, please email—and this box has been noted throughout the program today-- CDRH-EUA-Templates@fda.hhs.gov.

As we continue to hold these virtual town halls, we appreciate your feedback about the program series.

Please complete a brief survey which you may find at www.fda.gov/CDRHWebinar. Also, please remember to join us for the next IVD Town Hall that is scheduled for Wednesday, February 9, 2022. This concludes today's program. Thank you.

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