

**Virtual Town Hall #74
December 01, 2021**

Moderator: Joseph Tartal

Joseph Tartal: Hello, and thank you for joining us today. I am Joseph Tartal, Deputy Director in the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. And I'll be moderating today's program. Welcome to Virtual In Vitro Diagnostic IVD Town Hall Number 74 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 title 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 November 17th. We're hoping to post that by next week. The next and last IVD town hall for calendar year 2021 will take place in two weeks on Wednesday, December 15th. The next and last IVD Town Hall for calendar year 2021 will take place in two weeks.

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, Deputy Director of the Division of Microbiology Devices, also in OIR. We'll begin with opening 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 a little too detailed or test case specific that we will not address on the call. For those questions, we'll try to send our response in writing within a few days. If you submitted a question and do not hear it addressed, please look for a 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 and send it to that mailbox for an update. Last, then we'll open up to live questions. Please note that we are only doing live questions by phone. So please do not type anything into a Q&A box. With that, I will now hand this over to Tim for opening remarks. Welcome, Tim.

Timothy Stenzel: Thank you, Joe, and welcome everyone. Of course, the big news for this week is going to center around omicron. The FDA and other agencies within the federal government and state, local, and public health labs are very busy assessing the situation and putting plans in place to screen for omicron in the US. And just the general statement, we have done our typical bioinformatics search of all EUA authorized tests, and we have no certainty now that any test is negatively impacted by mutations seen in Omicron.

However, we have a fair amount of work to do to definitively say at the end of the day that there is no impact. We have already sent notifications out to key developers where we would specifically like them to assess performance for omicron. And we also note that all test developers are expected to do to their own evaluation for variant performance issues. Because there is so much concern about omicron, we certainly want you to go ahead and do your assessment. And if you haven't been contacted by an email, it means that we think that the risk is relatively low. However, if for your particular test, however, if you do discover something, please let us know as soon as possible, and we'll work with you on that.

One of the easiest methods to screen for omicron is through the so-called S-gene dropout. The best known widest utilized assay out there is probably the Thermo Fisher TaqPath combo assay. As we saw with alpha and have posted on our website already, that assay is able to detect the deletion 69 70 through the dropout of S, but the other signals are positive. So these are the best samples to send for sequencing to determine whether or not that sample is coming from a patient infected with the omicron variant.

And at this moment it's public health monitoring only. We know of no definitive decrease in vaccine or therapeutic efficacy. Obviously, separate efforts are going on for that. So we are encouraging all labs that can use a test that has the S-gene dropout signal when they can to test with that now until we get a good handle on omicron. At least there are over 20 tests that are able to detect the S-gene dropout. All of them have the S-gene design that Thermo Fisher has.

We are working on updating our FDA website with this information. Also look to the website for any updates on any tests that may see a decrease in sensitivity for omicron. And we will update that web page on an ongoing basis. So check back when you can. In all likelihood, we will do some sort of communication on that web page when it's first updated with omicron.

Let's see. Yeah, I think that's what I wanted to introduce and to get us kicked off here today. And then I'm going to turn it now over to Toby who's going to go through the questions we received ahead of time along with the answers. Thank you.

Joseph Tartal: Thank you, Tim. So we're going to go on to the emailed questions. And the first email question received for Toby is what are the recommendations for external controls?

Toby Lowe: Thanks, Joe. So generally, FDA recommends that external positive controls for point of care and CLIA high complexity and moderate complexity labs be approximately five times the LOD of your test in order to verify that the test is performing as intended. And any control that's used with your device that you recommend using with your device or include in your labeling for use with your device whether or not that's provided with your test kit should be validated in the context of your analytical and clinical studies. For molecular tests that are intended for at home testing, an external control is generally not expected but an internal control is expected.

And for a third party external controls that are labeled for IVD use and recommended for use with your test but are not included with your test kits, we do not expect those to be brought under the EUA holder quality system.

Joseph Tartal: Thank you. The next question: are early emergency use authorization manufacturers required to perform additional validation based on updated templates such as the recommendation in the October 6, 2021, molecular emergency use authorization template to evaluate each upper respiratory sample type?

Toby Lowe: So the recommendations that are provided in the EUA templates are updated based on a variety of factors throughout the pandemic and as things progress. Issuance of these updated recommendations in the EUA templates does not impact any previous authorizations. Unless they are revised or revoked, the previous EUAs are still valid as previously issued. We do continue to monitor tests and test performance post authorization, and we do reach out to an EUA holder directly if we determine that there's a need for further evaluation.

Joseph Tartal: OK, perfect. Next question: does the priority stated in the updated guidance regarding tests for which the emergency use authorization EUA request is from or supported by a US government stakeholder apply to additional EUA requests or EUA supplements for iterations of tests that were formerly funded by a US government stakeholder but is not any longer? I know there's a lot to that, so.

Toby Lowe: Yes, so generally we consider each submission independently when we determine the priority for review. So we consider when considering this particular priority, we consider whether the submission at that time is supported by a US government stakeholder.

Joseph Tartal: OK. Next question: will FDA accept new EUAs for combo COVID-19 flu A and B tests submitted after the 60 day window provided in the updated guidance?

Toby Lowe: So this one, I think this question demonstrates a misconception from reading the updated guidance. So the 45 day and 60 day time periods that are discussed in the updated guidance are specific to tests that are being offered prior to an EUA under previous policies. These time periods indicate the time frame in which FDA expects to receive an EUA request for those tests that have already begun being offered such that FDA would then not object to the test continuing to be offered during FDA review.

The guidance does not provide a time period during which new tests meaning those not offered prior to November 15th, 2021, need to be submitted to FDA. We intend to continue to accept EUA requests for COVID-19 tests and we'll prioritize review according to the priorities laid out in the 2015-- November 15th, sorry, the November 15th, 2021, guidance update.

Joseph Tartal: OK, thank you, Toby. And our next question is can developers leverage existing real time stability data for an EUA authorized point of care POC antigen test to support an EUA request for over-the-counter use for the same test? And is stability required for different kit size configuration?

Toby Lowe: So if the point of care test is identical to the over-the-counter version, then it is acceptable to leverage the same stability data. We would recommend that you provide a side-by-side comparison in which you demonstrate that any differences between the test kits would not be expected to significantly affect the stability. And we generally would not expect the test kit size to impact stability, so the different size configurations.

Joseph Tartal: OK, perfect, and that is the end of our emailed questions. And remember if your question was not answered it may have been again either very specific or case-specific, we will try to get a written response back to you in a few days. If you do not receive a written response, feel free to reach back out to the CDRH-EUA-Templates@fda.hhs.gov mailbox for an update. So thank you to everyone who emailed questions in, and please keep those questions coming in as we will prepare for the next town hall on December 15.

So now, we're going to transition the program to the live portion of Q&A. So at this time we're asking that if you have a question, please raise your hand. I will announce your name and invite you to ask your question. When I do that, please unmute yourself when you're called on to ask your question. And when asking your question, announce your first, last, and business name. Ask your question. Please keep it to one question only. If you have another question, you can later raise your hand again and come back up

through the queue. And please do not ask questions about specific submissions. Please reserve those questions for the EUA template email box or discuss with your reviewer.

So the first question is from Richard Montagna. I'm going to unmute you. Please once unmute you, unmute and ask your question. You've been unmuted.

Richard Montagna: Thank you, this is Richard Montagna from Rheonix. Despite the omicron situation, we like others had previously been asked to update our package insert as to how we deal with the known variants at the time. We did that. We sent it in I'm guessing around three or four weeks ago. And we were uncertain if we are allowed to just go ahead and use that new package insert or whether we need to wait for FDA to respond to us.

Timothy Stenzel: Kris, I know that we've received a number of these. Can you address that question?

Kristian Roth: Yes, thank you. You can imagine that there are quite a bit of backlog because folks have been responding to that. So we are trying to work through that as quick as possible. And I would say in this instance likely you should probably wait until we do have your new labeling kind of reviewed and up on the website, and you have heard kind of positively from us that that is the kind of EUA revision.

Richard Montagna: OK, well, thank you.

Kristian Roth: You're not alone. Because there's a quite of few folks that are in this boat.

Richard Montagna: OK, I'm sure. Thank you very much. And we will be responding to your requests on the omicron variant as well.

Kristian Roth: Great, thank you.

Richard Montagna: Thank you.

Joseph Tartal: Thank you, Richard. Our next question is from Annie Wright. I'm going to unmute you right now. Please unmute and ask your question.

Annie Wright: Hello, can you hear me?

Joseph Tartal: Yes.

Annie Wright: My name is Annie Wright, and I'm from Wondfo USA. I had a question about if you were because we're in the process of looking into submitting an OTC. But we are looking into because of the supply chain issues of having two different swab manufacturers, one alternate and then the one main one. So we were trying to figure out how we would design our studies. And so we were looking for some advice on how to because we were kind of thinking essentially of using the main swab and then having some sort of equivalency testing but we're not clear on what that equivalency testing would be for the alternate swab.

Timothy Stenzel: And so this is Tim. I just want to confirm this as an antigen over-the-counter test.

Annie Wright: Yes, it is.

Timothy Stenzel: OK, all right. And the different swabs are they the same material just by different manufacturers?

Annie Wright: I believe so. We have not-- I haven't looked into that material but should we look into that and do a comparison with materials and such?

Timothy Stenzel: Yes, that would be important. And if they are the same material, I would provide that in the submission. And you probably want to do just a quick check to make sure that the swab that you don't do your clinical studies with and your analytical studies with us still performs well in the test. Kris, do you have anything more specific about that? I don't believe a full clinical study is needed with those and bench experiment probably is fine.

Annie Wright: What kind of-- should we do like an LOD would be sufficient to show equivalency or some--

[INTERPOSING VOICES]

Timothy Stenzel: I want to be considerate of what we've been asking other developers to do here. And it potentially is not even something that we need to review if the material is the same. Kris, do you have any specifics right now or do we want to redirect this.

Kristian Roth: Yes, I mean, it's always safest to reach out to the inbox with these specific questions, and certainly if you're talking about a swab that has the same material, the same dimensions, typically that's kind of interchangeable from our standpoint with that kind of data. If there are changes you know, a spun polyester to a phone swab for instance, that's when we start talking about OK, well maybe even LOD study or some kind of other bench study to establish similar performance that's needed.

So I think really getting the details of those two different swabs would be your first step and then just letting us know that question from the inbox would be helpful.

Annie Wright: OK, great, we'll do that then thank you so much.

Joseph Tartal: OK, our next question is from Sarai Meyer. I'm opening up your line. Please unmute yourself and ask your question. Are you there? OK. I'm going to move on to the next question. The question up next is from ProterixBio. Please, when I unmute yourself also provide your name who's asking the question so you're currently on mute it. Please ask your question.

Najwa Lamnii: Hi, my name is Najwa Lamnii and I'm from ProterixBio. The question is we have submitted our notification, and we are on the notification list for the FDA and it was meant to offer a validated IVD serology assay as an LDT. But we have since validated the serology assay against the nucleocapsid protein as well. And that's meant like to potentially aid in distinguishing immune response to the prior infection versus vaccination. And we were wondering if we should submit a separate EUA for the nucleocapsid and RBD serology assays.

Timothy Stenzel: Toby, can you handle this one?

Toby Lowe: Sure, excuse me. So if those are two different assays and you are intending to offer both of them, then yes, we would expect to see two EUA requests, one for each test. If you have switched so

that you are no longer planning to offer the RBD assay, and you're only planning to offer the nucleocapsid assay, then you could just let us know that you want to be removed from the notification list without submitting an EUA request for the first one and then just submit your EUA request for the second one.

Najwa Lamnii: Thanks.

Joseph Tartal: Thank you. And our next question is from Dana Hummel. So Dana, I'm unmuting you right now. Please unmute yourself and ask your question.

Dana Hummel: Hi, this is Dana Hummel with MP Biomedicals. I have a question about the template for home use that came out on November 9th. And it says that you should enroll at least 10 positive individuals without symptoms or epidemiological reasons to suspect COVID if you want the asymptomatic claim. So I was wondering what is the FDA's definition of other epidemiological reasons to suspect COVID-19? And does that include anyone exposed? And then part two, sorry, I have background noise. there we go.

Part two of my question is, if we do enroll any asymptomatic patient who has been exposed or has epidemiological reason to suspect COVID, do we count them in the numbers for the symptomatic subjects or the asymptomatic subjects when we report PPA split out separately? Or do we just include them in the overall PPA and not include them if we split out symptomatic and asymptomatic?

Timothy Stenzel: Thank you, and I think we want to be precise on our answer here. So Toby or Kris, do you want to handle that?

Kristian Roth: I could start, but we're probably not going to be able to answer the question completely, just a couple of details there. So in the template, it does say 10 positive individuals without symptoms or other epidemiological reasons to suspect. So that's really the screening population, right, so it's not folks that are close contacts. It's not folks that are basically close contacts is kind of a differentiator there. So if it is kind of that screening population where you're taking all comers and there's really no kind of efforts to differentiate risk factors, then that really is kind of the screening population and what we'd be looking for in that in that study.

Dana Hummel: OK, if we ask them, if we ask them if they have been exposed or in close contact with someone, even if we're doing an all comers study, and they have been exposed, then do we need to exclude them, or can we keep them since it's an all comers study?

Kristian Roth: So barring any other input, I would say as long as it's not an exclusion criteria, you're fine to collect that information of course and it's certainly by nature of the pandemic some folks are going to have close contacts. But as long as it's not part of your exclusion or inclusion criteria, then that's the qualifier, but I think Tim had something to say, sorry.

Timothy Stenzel: Well, and Toby may have something as well.

Toby Lowe: Yeah, I was just going to say someone who has a close contact would fall under what we've been referring to as suspected of COVID. So the idea is that we would want to see your study stratified by those that are symptomatic or otherwise suspected of having COVID because of a close contact and those who are asymptomatic and have no reason to suspect. So as Kris was saying, the general screening

population where there's no reason why they're not testing because they think that they might have an active infection. They're testing because they're just doing routine screening.

Timothy Stenzel: You know, this is a difficult area, and I think the question really is because can count somebody who they identify doesn't have simple symptoms at the time. But they find out maybe in the enrollment process that they may have been exposed. Do they still qualify as an asymptomatic person for the asymptomatic count?

Dana Hummel: Exactly.

Timothy Stenzel: I mean, if the team's not ready to provide a definitive answer, we can get back and bring this up next call and get back to the specific person. But you know it's something that we definitely want to be clear on.

Toby Lowe: Yeah, I think that's probably an area where we could have further discussion. But generally, it's going to be where we want you to track as much detail as you can understanding that things are happening in real time and in a pandemic. So you want to track whether someone is presenting as symptomatic or asymptomatic and exposed or not a known exposure as much as possible.

Timothy Stenzel: Right, for this developer and maybe for others, we want to get a precise answer on whether that kind of person would qualify as the minimum 10 for asymptomatic. A lot of people are going to be exposed to COVID these days. Sometimes they're not going to know. Sometimes they might know. So I suggest if you could, Dana, to submit an email to template's email address. Ask to copy Toby, Tim, and Kris, and we'll drive to an answer here, clear answer, and we'll provide clarity as soon as we can to all the developers.

Dana Hummel: Thank you so much. I appreciate it.

Joseph Tartal: Thank you, Dana. Our next question is from Dr. Marilyn Freeman. I'm unmuting you now. Dr. Freeman, please unmute yourself and ask your question.

Marilyn Freeman: Thank you. We are the Public Health Laboratory for the State of Virginia, and we are a high complexity laboratory per CLIA that has validated per CLIA regulations and assay for whole genome sequencing of COVID-19 virus such that we can report back to clinicians as well as patients. And so I just want to get some clarity. If we have validated this method in this manner, are we still required to submit an EUA request to FDA to continue reporting these results to clinicians and patients?

Timothy Stenzel: Toby, can you handle that question?

Toby Lowe: Yes, so this would fall under the discussion in the updated guidance that talks about FDA review of EUA requests for tests that were offered prior to November 15th, 2021. And so since it sounds like you have not previously submitted an EUA request, we would expect you to submit one within 60 days of the release of that guidance so 60 days from November 15th. And then we would not intend to object to you continuing to offer that test while we review your EUA request.

Timothy Stenzel: And I would add that we want to make this as easy as possible for you in this situation. These are LDT lab situations where you have developed test, validated it, launched it without interaction with the FDA today. Go ahead. Don't try to fit it into any format and template that we've provided.

Simply make some sort of copy of what you have in your file. It may be in your CLIA records that the appropriate elements of that. Just copy it, scan it, whatever, and send it to us as is. You may want to attach a cover letter that explains how to organize or something like that.

But we want to make this as easy as possible for you. So we don't want you to have to manipulate your files and data into some format that we typically receive. So we're offering that to LDT labs who have launched their tests already. Does that address your question?

Marilyn Freeman: Yes, it does, just a follow up if you don't mind, if we revert to only reporting to public health departments only, is that EUA still required?

Timothy Stenzel: No. Sequencing based assays or any other these kind of assays that are doing population screening or anything like that aren't reported back to clinicians or patients for clinical purposes, you know they don't fall within for this pandemic at least FDA per you or we're not saying that they need to come in. We fully support the use of these kind of methods to help us track this from a public health perspective.

Marilyn Freeman: Thank you.

Joseph Tartal: Thank you. And our next question is from David Freedman I'm unmuting you right now. Please unmute yourself and ask your question.

David Freeman: Good afternoon. David Freeman, Lighthouse Labs, my question is actually a little bit of a review. I had some technical issues and would like to go over the 45 and 60 day commentary on the fourth email question. Could you provide a little bit more detail on your response to that? Thank you.

Toby Lowe: Yeah, happy to do so. So the 35 day and 60 day time periods that are discussed in the guidance are four tests that are offered prior to an EUA under the previous policies as discussed in the updated guidance. So those time periods are referring to the time frame in which FDA expects to receive an EUA request for those tests such that FDA would then not object to the test continuing to be offered during FDA review. These policies are discussed in Section 4c of the November 15th guidance. And there's also a flowchart that shows how they play out in Appendix B of the guidance.

David Freeman: And just to confirm, what, and I know you've said it twice now. I don't mean to make you repeat, but if we are pending an EUA review, we can continue to utilize the tests?

Toby Lowe: If you were offering the tests for clinical use prior to November 15th under one of the policies in the previous guidance or as an LDT following the August 2020 HHS statement, then as outlined in Section 4c of the November 15th guidance, FDA does not intend to object to you continuing to offer that test while your EUA is being reviewed or while you're preparing to submit it and then it's being reviewed as outlined in the guidance. So there are some stipulations that go along with that are discussed in more detail in the guidance.

David Freeman: Thank you.

Joseph Tartal: Our next question is from Rainier Ziermann. I'm unmuting you right now. Please unmute yourself and ask your question. They look like they just dropped off. No please unmute yourself and ask your questions.

Rainier Ziermann: Can you hear me?

Joseph Tartal: Yes, but you do have some playback going on.

Rainier Ziermann: Can you hear me better now?

Joseph Tartal: Yes, that's better.

Rainier Ziermann: Hi, thank you, sorry about the technical issues. This is Rainier Ziermann. I have a question about the use of the Abbott alinity SARS-CoV-2 assay as a comparative test for clinical study for a molecular test. Is that acceptable by FDA?

Timothy Stenzel: Yeah, we don't want to call out any particular test in a public meeting like this. So do send your question to the email template. If you've already submitted it for this week. I think we had a similar question submitted prior to the meeting at the top of the call we said that if we didn't get back to you. And we just want to be fair to all test developers and not just isolate response for one developer.

Rainier Ziermann: Sure, I understand. Thank you. Can I have a quick follow up question? Dr. Stenzel mentioned earlier for those manufacturers who want to convert an LDT to an EUA for an assay that's on the market right now not to use necessarily the template but just send the validation data that exists based on the CLIA laboratory. Is there a contact available for companies to talk to about more specifics about this. Because there's no time to really do a pre-submission right now in order to meet your 60 day deadline. And so I'm just wondering if you can contact somebody for some specific questions about what to include in that submission.

Timothy Stenzel: Yeah, so you can use the template if you want. But if it's easier just to scan the documents that you use to record your validation, and you can send an email to the template's email address, Toby? You can respond to that later. Let us know that you do have an LDT, and you will be submitting and you certainly can ask any questions of the template email at the template email address that you have. But you can look at the templates on the FDA website and see what kind of things we're looking, so be sure and if you have them for sure and scan them and send them to us.

There may be elements you know that you have in your particular CLIA file that we're not going to be looking for. So and then if there's something that isn't there, we will follow up or someone will follow up and say, hey, do you have this, which you may have left off. So our focus here and because we're allowing this non-standard format, which makes it a little bit harder on our reviewers because everyone's going to be a little bit different. We want to make it this very easy for LDT labs who have not previously submitted their application to the FDA to go ahead and just provide what they've already had in the format they have it for CLIA. And we'll review that.

If there are questions, or if there are potential concerns about an application, our focus is going to be working with that those individual labs, try to address those questions and work with the labs. We are overall wanting to maintain the access to testing that currently exists, and we want to give every opportunity for these labs to address any questions that we have.

Rainier Ziermann: Great, thank you very much. So I just will send an email to the template's address and ask for guidance. Thank you.

Toby Lowe: And just to expand a little bit, absolutely, if you have a question about what you're going to submit, send it into the mailbox and they'll try and get back to you as quickly as possible. But to Tim's point, the template does include everything that we are looking for in an EUA request. And if you're able to use the template, that certainly will streamline the review of your EUA request. If that's a big lift for your lab to complete the template, then you can just send in the validation documents that you have on record in your lab already, and we'll take a look at those.

Rainier Ziermann: Great.

Timothy Stenzel: That's the last choice. That's the last choice on what we can do there. And we want to provide maximum flexibility. Thank you.

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

Vitali Karaliou: Hi, everybody. I'm Vitali Karaliou from Biotech in Butler University. My question is about pooling strategy. Is it strong requirement for EUA is by itself it may decrease some sensitivity. And do you require just a brief description of this, or you need to provide clinical data? Because it may prolong the clinical studies done.

Timothy Stenzel: Yeah, are you you're an LDT lab or a kit test developer?

Vitali Karaliou: It's test developer.

Timothy Stenzel: I'm sorry, say that again.

Vitali Karaliou: Test developer.

Timothy Stenzel: A kit test developer or an LDT lab?

Vitali Karaliou: Kit test developer, sorry.

Timothy Stenzel: OK so absolutely, there are situations where we want to see data. I think Kris was probably most up to date on this. What we've seen is is properly developed and validated pooling strategies that don't pool too many samples for the given technology, especially for molecular tests has proven to be quite sensitive. And so in order to get greater testing capacity and throughput, those kit developers and those labs that want to utilize pooling, it certainly isn't required to pool, but if you want to and you can and it expands testing opportunities, We're all for that, and we'll work with you. So but as far as I don't know Kris you have on the top of your fingertips for kit developers what the various options are.

Some of them may be less challenging than others. Kris, you want to make any comments about pooling or we could just refer to the templates. Because it's pretty well laid out in the template.

Kristian Roth: Yeah, thanks Tim. I would just refer you to the template. It's not a requirement. There's an option. Of course, you can just come in with your single test, single sample test first, and then work on pooling as the data allows. And I think that a number of folks have done that. And so that would probably be your quickest path to market is to get those individual sample validations done first. And then you can work on pooling afterwards.

Vitali Karaliou: Great, thank you so much.

Joseph Tartal: Our next question is Sarai Meyer. I'm unmuting yourself now. Please unmute yourself and ask your question.

Sarai Meyer: Hello, can you hear me?

Timothy Stenzel: Yes, yes we can hear you now.

Sarai Meyer: OK, so I had a question regarding home tests that don't have validated external controls with their authorization. If a CLIA waived point-of-care lab would like to validate an external control to use with said home tests, how should they go about doing so?

Timothy Stenzel: Are you the developer or are you a CLIA lab?

Sarai Meyer: We're the developer, but we're fielding questions from a CLIA lab.

Timothy Stenzel: Kris, do you feel like this question we can answer on the phone today?

Kristian Roth: I'm a little bit so that probably not, but I'm just trying to understand the question a little bit better. So the CLIA lab would purchase the test, and then they would-- the lab themselves would validate controls for use with that test for use only in that particular laboratory. Is that the question?

Sarai Meyer: Yes, there's a developer well, there's a potential developer lab that would like to use it across a lab system, and they would like to validate a control to use with it.

Timothy Stenzel: And particularly--

Toby Lowe: A point of care?

Sarai Meyer: Yes this would be a point of care.

Toby Lowe: So it's at a CLIA certificate of waiver site?

Sarai Meyer: Yes, CLIA waived setting.

Timothy Stenzel: So this has already authorized tests for the home and--

Sarai Meyer: Yes.

Timothy Stenzel: And you want to make it available in point-of-care setting. So we typically if that request comes in from a developer at the time of authorization, we would include labeling for point-of-

care. And I think there may be at least a post-market commitment to provide external controls for point-of-care sites. Toby or Kris, do you want to expound on that? I do think you should send this question to your previous reviewer for the authorization and/or the template's email box so we can get back to you specifically.

Toby Lowe: Yeah, I think that probably the simplest thing would be for the developer to get this added to the authorization if the external control is being validated for point-of-care use. I think that there is-- we don't like to speak for our CMS colleagues on this call, but our understanding is that certificate of waiver sites under CLIA are required to perform a test according to the manufacturer's instructions for use. So I think that would cause some issues if they wanted to use a control that is not in the instructions for use.

Sarai Meyer: All right, thank you.

Joseph Tartal: Let's go to our next question. Denise Toney, I'm going to unmute you. Please ask your question.

Denise Toney: Hi Denise Tony from the Virginia State Laboratory. Our lab is working with an academic laboratory partner that has developed point-of-care tests that they would like to deploy for use in schools across our state. If they are not able to meet the high manufacturing criteria that are stated in the new guidance, is it correct to advise them that FDA will not review an EUA if they submit it?

Timothy Stenzel: Well, that is our desire is to foster development and spend public health resources to review tests that will meet the national need. However, the developer can certainly come directly to us. There are also a programs funded by the US government that if the US government if it's BARDA and RADx NIH want to fund manufacturing expansion something like this, it could change the situation. So I would hate to say no directly on the phone here. So I think directing them to send an email to our template's e-mail box with some information, we can certainly provide specific feedback to them you know after finding out some more details from them.

Denise Toney: Thank you.

Joseph Tartal: Thank you, Denise. Our next question is from David Freeman. I'm unmuting your mic. Please unmute your mic and ask your question.

David Freeman: Hello, it's me again. I wanted to pick your brain about the second emailed question. If you can't tell I have some early technical difficulties and would love to have that expounded on. Thank you.

Timothy Stenzel: Do we know what question he's talking about?

Joseph Tartal: So it's the second one in the order?

David Freeman: Yes sir.

Toby Lowe: It's the question about validation, about previously authorized tests and validating to the new templates. Is that the question you're referring to?

David Freeman: Yes ma'am.

Toby Lowe: OK, so what we indicated for that question is that the recommendations provided in the EUA templates are updated throughout the pandemic and based on a variety of factors. So issuance of updated recommendations in the EUA templates does not impact any previously issued EUAs. So unless an EUA is revised or revoked, the previous EUAs days are still valid as previously issued. We continue to monitor tests and test performance on an ongoing basis after authorization. And we reach out to an EUA holder directly if we determine that there's a need for any further evaluation.

Timothy Stenzel: Yeah, so I'll also just maybe respond in a slightly different way. Our thinking has evolved as the science has evolved, and unless we see something with a particular test that was authorized before or there's a particular issue that we feel needs to be addressed, we're not going to require all 400 plus test developers to revalidate their test. But as we go forward, since there are so many tests already authorized and their thinking has evolved, that new submissions or submissions under review, this will be discussed during the interactive process.

David Freeman: And well, thank you for your patience.

Timothy Stenzel: You're welcome. Does that address your question well enough?

David Freeman: It does. It does.

Timothy Stenzel: OK.

Joseph Tartal: OK, thank you David. And we'll take one more question from when Wenli. I'm Opening your mic. Please unmute yourself and ask your question.

Wenli: OK, thank you for taking my question. So I have a question about the clinical study design for OTC antigen test. Is the enrichment strategy still an option for that or not?

Timothy Stenzel: Yes, but that's something that we want to-- Yes, you hear me? This is Tim. Yes, it's something that we're-- can other people hear me?

Wenli: I'm sorry, yeah I just, yeah, I just heard you. Sorry, Tim.

Timothy Stenzel: OK so we're open to enrichment schemes. You know unfortunately the testing positivity rate out there now is pretty high in the 5% to 10% range, so it's a little bit easier. But we are open to enrichment schemes. We just want to make sure that doesn't introduce bias towards the candidate test making it look better than it really is. So that's best handled with the review team through the template's email box or through a submission of a pre-EUA with a specific question on enrichment for an OTC test. And I would provide your study design for that enrichment and your justification for why it is not going to bias in favor of the candidate test. And we're open to those questions but want to assure that the data that's collected in such studies accurately reflects the true performance of the test.

Wenli: Thank you.

Joseph Tartal: OK, we're almost out of time but we are taking one last question from Ivo. I'm going to open up your mic. Please quickly ask your question. OK it doesn't look like they're there. So I'm going to move forward with the program. So thank you everyone. We greatly appreciate your participation today.

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 titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. We're working on posting all the programs as soon as possible.

For additional questions about today's town hall and COVID-19 IVD topics in general, please email the 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 can find at www.fda.gov/cdrhwebinar. Last as a reminder, please join us for the next IVD town hall and the last four calendar year 2021 scheduled for Wednesday, December 15th. Thank you, and this concludes today's program.

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