

## **FDA Virtual Townhall**

**Moderator: Irene Aihie**

**May 19, 2021**

**12:15 pm ET**

**Coordinator:** Welcome and thank you for standing by. At this time, all participants are in a listen-only mode until the question-and-answer portion of today's call. During that time if you would like to ask a question, please press Star 1. Today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn the meeting over to Irene Aihie. You may begin.

**Irene Aihie:** Thank you. Hello. I am Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 56th in a series of Virtual Town Hall meetings to help answer technical questions about the development and validation of tests for SARS-CoV-2 during the Public Health Emergency.

Today, Toby Lowe, Associate Director of the Office of Invitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality and Dr. Timothy Stenzel, Director of the Office of Invitro Diagnostics and Radiological Health, both from CDRH, will provide a brief update. Following opening remarks, we will open the line for your questions related to the development and validation of tests for SARS-CoV-2. Please remember that

during the Town Hall, we are not able to respond to questions about specific submissions that might be under review. Now I give you Toby.

Toby Lowe: Thanks Irene. Hey everyone, thanks for joining us again this week. Excuse me. Every week I'm always amazed when I hear Irene announce the number of the Town Hall that we're on. It's been quite the, the year, plus a bit at this point. So, I have one update to give this morning, or this afternoon, and then I'll go through some of the questions that we received in advance.

So, first I just want to highlight that right before the Town Hall, a new Safety Communication was posted discussing the use of antibody tests after COVID-19 vaccination. And specifically, recommending not to use antibody tests to assess immunity after COVID-19 vaccination. So, those of you on this call most likely get the emails that go out with updates when we put out actions like this. So, you probably have gotten that just a short while ago, and if not, it is found on our Web site under Medical Device Safety Communications. And there was also a press release issued or rather an FDA in brief press statement. So, you can find that on our Press Announcements page as well.

And with that, I will switch over to some of the questions that we received ahead of time and I'll go through those. So, the first, the first question that we got in is related to modifications to an authorized molecular SARS-CoV-2 assay. Specifically, to speed up the processing time by implementing a software change to a fully automated system to allow the system to simultaneously perform some steps that were previously performed sequentially.

The question notes that the change would be implemented through their design control process, design change control process, and validation data would be documented in their quality system. And that there were no changes

to the assay design or reagents so they're asking whether they can put out that change without further amendments to their EUA.

So, that will depend a little bit on the changes that are made if parameters to the test which is the temperature, dwell times, ramp rates, or the extractions speeds are changed. Then we would expect performance to be impacted.

And in that case, we would expect a supplement to an EUA request. If your proposed change did not impact the performance of the device or change to the claims in the intended use or introduced substantially new information such as the addition of new hardware to support the software change, or any additional steps the user needs to take into the instructions for use or any of the authorized labeling. Then the change could be made without further amendment. An example to that would be if the reaction steps used the same parameters on a per-sample basis. Then there would be little risk that performance would be impacted.

The next question that we have is asking if we can confirm that the FDA is no longer accepting EUAs for COVID-19 antibody tests. And if that is confirmed, would EUAs for other types of COVID-19 tests be affected by this? I can confirm that that is incorrect. We are still accepting EUA requests for COVID-19 antibody tests as well as molecular and antigen COVID-19 tests. As we discussed at the Town Hall previously, we do continue to prioritize reviews based on public health needs and we generally prioritize tests that increase capacity or access including tests for use at the point of care and home collection and for cases at home. And we will continue to update, you know, on our priorities as we go forward.

The next question is about CLIA categorizations. In our previous Town Hall, they're referencing discussion about the fact that there is no formal CLIA

categorization during an EUA and instead, that FDA uses a deemed as waived approach. They're asking whether this deemed as waived approach can be applied to a new assay on a new instrument that FDA has not previously reviewed. Or whether or FDA would require a traditional pre-market review to establish CLIA moderate complexity or CLIA waived status. So, I can clarify that we have, and we will when appropriate authorize tests under an EUA for use at the point of care. Even in situations when the instrument is new and has not been previously reviewed by FDA. Tests that we authorize for use at the point of care under EUA are considered to be deemed "waived" for purposes of the Emergency Use.

So, what that means is that in the EUA Letter of Authorization, we indicate the specific authorized setting and for point of care tests we indicate that they can be used in settings that are operating under a CLIA Certificate of Waiver. They, those tests are not officially categorized as "waived" because they are only authorized for use during the Public Health Emergency. And after the emergency is over, the assay and the instrument will only be able to continue to be used in the same setting after obtaining 510(k) clearance and CLIA waiver. And, you know whatever transition may be in place at the time, at some future time, when the emergency is declared to be over which we don't expect to happen anytime soon. But just clarifying that the, the deemed waived, is only for the emergency use.

And we do consider similar, you know, similar issues related to the tests when we, and the instrument, when we're considering whether to authorize for use in point of care. Just as we do when we do a CLIA categorization, so we look to make sure that if demonstrated to be simple to use and with additional, and that there's additional data demonstrating, excuse me. That there's an insignificant risk of erroneous results when used by a non-laboratorian.

And we do have examples of tests that we have authorized for point of care use during the emergency that did not previously have a CLIA categorization prior to the emergency. Some of the examples for molecular tests are the VISB Medical Point of Care Test, the Lucira COVID-19 Test, and the Q COVID-19 Test. And then for antigen tests, we also have similar examples in the Lumira Dx Luminostics and Cell Trion Antigen Tests.

The next question that we have is related to turning towards full submission, 510(k) submissions, for molecular SARS-CoV-2 tests. And asking about analytical studies to support a 510(k). The question is specifically asking about clinical matrix studies. And whether clinical matrix is only required for substance stability and fresh versus frozen validation studies and whether specimens for those studies can be contrived in clinical matrix. So, generally we do require that analytical studies be performed with naturally occurring clinical matrix. In circumstances where naturally occurring clinical matrix is not available or is difficult to obtain, a synthetic matrix may be used for selective studies other than specimen stability and LOD. Provided that the performance observed with such a matrix is similar to that observed with naturally occurring specimens.

So, when designing a simulated matrix, we recommend that each component of the matrix should simulate a component of a true clinical specimen. For example, in the formulation of a simulated throat swab matrix, you should consider using a cell phone use such as a pig gastric mucin. Because they predominate in the pharynx and are known to aide in bacterial preservation. Your simulated matrix should not contain components that do not mimic properties of a clinical matrix, especially if they are commonly used for aiding in analytic extraction or preservation.

As appropriate, you should also consider each of the specimen collection and transport devices with which you wish to claim compatibility of your device and provide data to support their use. A simulated matrix equivalence study should be performed to compare the assay performance in synthetic and naturally occurring matrix. And that testing should be performed in parallel at the same target levels in both simulated and naturally occurring matrixes. In order to demonstrate equivalency, you should observe the expected proportion of positive results at each target level in both sample types. And as we've previously suggested in these Town Halls, we do recommend that if you intend to pursue a 510(k), that you submit a pre-submission to discuss your validation approach.

All right. The next question that we have is about home use antibody tests and asking specific questions about the validation and prioritization. So, unfortunately since we have not yet finalized a template for COVID-19 serology home use self-testing, we're not able to comment further at this time on specific validation study recommendations. And we would recommend that you reach out through a pre-EUA or if you would like to pursue a de novo or 510(k) through a pre-submission to further discuss your approach.

Next question that we have is about a SARS-CoV-2 antigen test with an asymptomatic claim and this is for a high-volume lab test not point of care or over the counter. Asking about, what the minimum requirements for performance for asymptomatic and criteria for enrollment in the study. So, for moderate or high complexity labs, the performance expectations for symptomatic and asymptomatic are the same, 80% PPA. And for enrollment of asymptomatic individuals, we would expect that they are free of any symptoms of SARS-CoV-2 infection for at least two weeks prior to enrollment and testing, if not known to be previously positive. And as part of your clinical study protocol and data, you should document in detail how

individuals were screened and confirmed to be asymptomatic and supportive of the proposed intended use.

We received a question asking if there is a public list of CLIA high complexity labs in the US or a way to find or contact high complexity labs in the US that might be willing to perform COVID studies for IVD test developers. The CLIA program, the lab certification portion of the CLIA program, is run by CMS. They can be reached by email at labexcellence@cms.hhs.gov, that's labexcellence as one word. And additionally, there is information about CLIA labs on the CDC Web site. If you Google CLIA Lab Lookup, it would generally be the first site that pops up is the CDC lab lookup database. If you're having trouble finding it, you can email the CMS email address that I just mentioned, or you can email us, and we can send you that link. But I do want to note that the CLIA lab lookup does not specify whether a lab is high or moderate complexity. They only list the type of certificate such as a Certificate of Accreditation or compliance that the lab has.

And the last question that we have for, for these pre-sent questions, is asking about home collection kits and whether a traditional 510(k) submission is the best or only option for home collection kit approval? And whether there's a guidance document available that would make the abbreviated 510(k) case submission a possibility.

So, assuming that this question is about home collection for SARS-CoV-2 tests, we have published a home collection molecular diagnostic template for EUA submissions. Which outlines the recommendations for an EUA request, excuse me, for home collection kits and we do not have any further guidance regarding 510(k) specifically or abbreviated 510(k)s. We have however authorized several home collection kits under the EUA and you can also refer

to the authorization documents on the EUA Webpage for additional information there. And with that, we can turn it over to live questions.

Coordinator: Thank you. We will now begin the question-and-answer session. If you would like to ask a question, please press Star 1. Please unmute your phone and record your first and last name clearly when prompted. Your name is required to introduce your question. To withdraw your question, you may press Star 2. Once again at this time if you would like to ask a question, please press Star 1. And our first question is from Jackie Chen. Your line is open.

Jackie Chen: Hello. Good morning. I have a question about the safety communication. Can you hear me?

Dr. Timothy Stenzel: Yes.

Jackie Chen: Hello? Okay. Perfect. I have a question about the safety communication that just got out this morning that was about the antibody tests that are not currently recommended to assess antibodies after COVID-19 vaccination. My question is, how about neutralizing antibody tests that demonstrate correlation to the plaque reduction neutralization test method? And also, if the print correlation is not sufficient, then what kind of clinical validation is needed? In particular, I'm interested to know how long of a longitudinal study is needed to demonstrate immunity or the protection from SARS-CoV-2? Thank you.

Dr. Timothy Stenzel: Yes. So, just to clarify, we are accepting serology submissions as Toby mentioned at the beginning and these are to detect antibodies, the presence of antibodies, to SARS-CoV-2. And we are certainly accepting neutralizing antibody submissions that, you know, that remains a priority for us along with I would say truly quantitative serology tests now that there's an International standard. What we don't have is data to support say the level of antibodies

that are present to SARS-CoV-2 and in the presence of neutralizing antibodies and the level of immunity.

The US Government is funding, you know, several studies to address this question. It is an important question and certainly developers can approach this as well if they wish. You know what we're really looking for is data that tells us about, you know, immunity. What is protective, you know, and what's the correlate to the neutralizing antibodies or the level of a truly quantitative antibody test, you know, to immunity. Toby, do you have anything else to add?

Toby Lowe: No. I think that's, you know, that's exactly right. We just don't, we don't know yet, so we don't, we're not at this point able to recommend that, that serology test be used in that way.

Dr. Timothy Stenzel: So, also developers that are interested in this topic. They can, you know, put together, you know, a validation study to accumulate this data and we encourage you to send us a pre-EUA with your plans to have us review that. The amount of data though that may be needed to properly assess immunity may be more than a single developer is willing to do. We'll just have to see. We'll have to see the results of the studies and many studies that developers perform in this area.

Jackie Chen: Thank you.

Dr. Timothy Stenzel: You're welcome.

Coordinator: Our next question is from Billie Ward. Your line is open.

Billie Ward: Hello. Thank you for taking my question. My question relates to who can sponsor an EUA and specifically, with regards to industry sponsors. My question is whether the agency expects only the product manufacturer to sponsor the EUA? Or if the FDA would accept and consider an EUA submitted by a distributor? Whether that be individually or on behalf of the manufacturer. Thank you.

Dr. Timothy Stenzel: Yes. We've authorized tests that, I think have been submitted by distributors, US distributors, and that is completely legitimate. We would prefer that your test developer doesn't have multiple US distributors submit applications to the FDA. That just makes our job harder because it doesn't really make sense for a single assay to be submitted in the US to have more than one set of validation data submitted. So, but, you know, that's also allowed, I'm just recommending that, that if the test developer wants to launch in the United States and work with a number of distribution partners. That they work that out and perform one submission, that would be ideal. Toby, anything to add?

Toby Lowe: Yes. I would, yes, I totally agree with that, with that approach, and just want to clarify that whoever does submit the EUA request is taking regulatory responsibility for that test. So, if the distributor is submitting the EUA request, that distributor would become responsible, you know, sort of quote unquote as the test developer, as the manufacturer, for all aspects of the test from a regulatory perspective. Which is absolutely acceptable from, from FDA's perspective. It just is important to, to be aware of, as the sponsor of an EUA and, you know, as Tim said we definitely prefer when a single submission is submitted for a test. And, you know, whoever it is that is submitting it manages the relationship with distributors rather than multiple EUA requests being submitted for the same test.

Billie Ward: Great. That's helpful. Thank you.

Toby Lowe: Sure.

Coordinator: Our next question is from Kristen Bancard. Your line is open.

Kristen Bancard: Hi. Thank you for taking my question. We're planning to submit a 510(k) for Molecular SARS-CoV-2 RT PCR test with saliva collected in a sterile container without preservatives as a specimen type. And so, is the indication for generic sterile container acceptable? Or does the specific device need to be validated for use with the assay?

Dr. Timothy Stenzel: Toby, you typically take this sort of question, you know, do you want to take this one?

Toby Lowe: Sure. I think this is something we can discuss with you further during your submission. We would want to see how you have validated the test and whether it's been validated with a single specific container or with a broad range of containers? And, you know depending on specific details about your test and about the proposed use we may have some more recommendations as we start working with you directly.

Kristen Bancard: Okay. Great. Thank you.

Coordinator: Our next question is from Sheree Kuja. Your line is open.

Sheree Kuja: Hey, good afternoon, Tim, Toby. Thank you all for all the hard work you guys are still doing on this pandemic. I have a very simple question which is, we're trying to develop a SARS-CoV-2 assay and we were looking at the reference panels that you guys are giving out to EUA authorized companies to test out.

And we couldn't understand how you defined NDU per ml in that reference panel? And also, I was looking for to see if the protocols that you guys want users to follow is sort of available online so we can download and follow it according to FDA's recommendations? Any advice you could give on this would be helpful. Thank you.

Dr. Timothy Stenzel: Yes. I would reach out to your lead reviewer for your EUA authorized test, that is if you haven't already been in direct contact with the FDA reference panel team. They can connect you with the FDA reference panel team and provide some more information. So, NDUs are, have to do with a subjective number based on the test that we use to assess the panel at the FDA. It is an average of a number of different molecular assays. So, it is not just, it's not an average, it's a compilation of multiple different targets within the genome of the virus. In order to get, you know, a very reliable nucleic acid detection assay result. So, it is, it is in some ways an artificial construct that shouldn't be compared directly to a typical LOD assessment and isn't intended for that purpose. So, hopefully that addresses your questions.

Sheree Kuja: Oh, yes, we haven't yet submitted an EUA. We are in the process of developing it. We thought that if we went with whatever FDA's proposing, it might be clearer. But I obviously our original plan was to do the LODs on say, a few per ml and when we saw the reference panel information, we thought that we might be able to do it the way the FDA would like to see it. That's why I was asking the question.

Dr. Timothy Stenzel: Yes. Yes. So, and I meant the NDUs is a subjective measure not an objective measure. It's, but it's independent of a true LOD assessment is done in the same way that you do this. And, you know for developers, for termination in their analytical studies of an LOD, they, you know, we recommend they follow the templates for the particular tests that you're

running. And when we have not been using the FDA reference panel for that purpose. The reference panel in fact is typically only provided to developers that have achieved an EUA authorized test. And it's at that point that they get put on a list for the reference panel.

Sheree Kuja: Thank you.

Coordinator: Our next question is from Elizabeth Burnilly. Your line is open.

Elizabeth Burnilly: Okay. This is with regard to post 510(k) clearance or post EUA 510(k) clearance for purposes of that. Are COVID-19 direct to consumer self-collection kit considered a device? Like are they always considered a device?

Toby Lowe: Is what always considered a device?

Elizabeth Burnilly: A direct to consumer, a COVID-19 direct to consumer self-collection kit.

Toby Lowe: Yes. That would be a device.

Elizabeth Burnilly: Okay. Does a COVID-19 collection device require 510(k) clearance post EUA? Is it required given the following scenario, using, it's used by a single laboratory with a laboratory developed test, nonprescription, direct to consumer, and self-collection?

Toby Lowe: A test for, excuse me, a test for non-prescription, self-collection, at home.

Elizabeth Burnilly: Yes. But it's.

Toby Lowe: But home collection kit.

Elizabeth Burnilly: With a laboratory developed test?

Toby Lowe: So, the, the home collection kit is not considered to be a laboratory developed test and would, would require authorization and clearance. And accordingly, laboratory developed tests are under, my understanding, from my CMS colleagues is that they do require an order by a physician.

Dr. Timothy Stenzel: And if I'm hearing correctly.

Elizabeth Burnilly: Okay.

Dr. Timothy Stenzel: Yes. This sounds more direct to consumer than even OTC only because it's not selling a device over the counter and handing a test device over the counter. Which at least in the terminology for the pandemic, it's only test kits that are sold over the counter as over the counter and collection kits is direct to consumers.

Elizabeth Burnilly: Okay.

Dr. Timothy Stenzel: And yes, Toby is correct, that, well, anything direct to consumer is not considered an LDT and then also, anything that is collected at the home does need specific authorization. However, I thought I heard and correct us if you're wanting to know about 510(k) pathways to add and seek authorization for a home collection kit, is that correct?

Elizabeth Burnilly: What I'm trying to determine is if that's absolutely necessary for every direct-to-consumer self-collection kit and you're saying, "Yes, it is". And in fact, even the test if it's non-prescription, needs to be 510(k) cleared. Am I correct on that?

Dr. Timothy Stenzel: In order to convert to a full authorization on any, any test, and including a home collection test with a home collection kit. Would, you know if it's molecular at this point would be a 510(k) because there's already been one Denovo that's molecular. And yes, we consider all home collection kits are not considered LDT's. And so, whether they're for the pandemic or for some other purpose submission to the FDA is important.

Elizabeth Burnilly: Okay. And even in LDT, if it's direct to consumer, meaning that the PCR test is LDT. If you're collecting it direct to consumers, that also needs to be 510(k) cleared or am I incorrect on that?

Dr. Timothy Stenzel: The direct-to-consumer aspect of this takes it out of the realm of an LDT.

Elizabeth Burnilly: Okay. Okay.

Dr. Timothy Stenzel: And it is a device and it's, important to get FDA authorization before launch.

Elizabeth Burnilly: Thank you.

Coordinator: Our next question is from Thomas Rhodes. Your line is open.

Thomas Rhodes: Hi. Thanks for taking my question. In light of the discussion about 510(k) submissions or full authorization for some COVID tests, potentially in the future. After one or more tests receives full authorization, will the pathway for EUA authorizations still be open for other similar PCR or antigen COVID tests?

Dr. Timothy Stenzel: Yes. In short, yes, absolutely. As long as an emergency is open and declared and, you know, the FDA intends to continue to accept EUA

applications according to the priorities that we've set. And those priorities can change and may be more focused depending on how long this lasts and how long the emergency lasts. And the law does and gives quite a bit of flexibility around, you know, decisions about, you know, what tests they'll actually consider.

For right now, our priorities have remained the same. We're looking at expanding access. We're looking at, you know, the accesses thorough extremely high input, central lab tests, particularly molecular diagnostic tests that have pooling and screening claims. Point of care, and particularly diagnostic tests in the home and over, including Rx, and over the counter. So, those are typical antigen and molecular assays that are of the highest priorities. All of those are designed to expand testing access, making school reopening's, or continued openings and workplace continued openings, and workplace reopening's as easy and safe as possible.

Let's see, there was another component of that. Oh, I did want to reiterate that those that are interested in full authorization, that they, it's not too late to be thinking about it now. But I wouldn't delay much further about doing those studies and we do recommend that pre-submission which we are receiving and reviewing for COVID. I'm not sure if I answer every nuance of your question. I'll just pause there.

Thomas Rhodes: Yes. That answers the question. Thank you very much.

Dr. Timothy Stenzel: You're welcome.

Coordinator: Our next question is from Bridget Bondock. Your line is open.

Bridget Bondock: Thank you for taking my question. During the May 5 Town Hall, there was a question related to FDA's willingness to consider home use, multi-analyte tests for SAR-CoV-2 and influenza. And the response is that FDA would consider a prescription home use, multi-analyte test. Building upon that in an effort to drive greater acceptability to these types of tests, would FDA consider an authorization of a direct to consumer, at home collection, multi-analyte tests for SARS-CoV-2 and influenza?

Dr. Timothy Stenzel: We've certainly authorized home collection from multi-analyte. I'm not remembering, hopefully Toby knows better than me. If we've authorized an OTC home collection, multi-analyte kit. Toby, do you remember?

Toby Lowe: Excuse me. I don't believe we've authorized a non-prescription, multi-analyte test at this point. Generally, there are no recommendations to test asymptomatic individuals for flu which is one of the reasons why we've kept that to prescriptions.

Dr. Timothy Stenzel: So, you know, I think that's the best justification for not going the OTC route or the serial testing route, other than directed towards SARS-CoV-2. But certainly, symptomatic panel tests that expand access for SARS testing and reduce the need for performing multiple tests on individuals. As long as it does truly expand access, that would be home collection, Rx home collection, point of care. And high volume, extremely high-volume central lab tests are still open. If someone is symptomatic, yes, it could be something else, typically is these days, and but, OTC has essentially no controls other than labeling on what the test is used for. So, right now, we're sticking to Rx.

Bridget Bondock: Thank you.

Coordinator: Our next question is from Natalia. Your line is open.

Natalia: Hi. How are you? Thank you very much for taking my question. My question was around the moderate to high complexity laboratory antigen tests. And what we're kind of trying to figure out is there any specific requirement that the FDA is looking for, for the NPA or specificity requirement? I know we touched on the 80% sensitivity, but we wanted to know if there is any kind of requirement around specificity in particular?

Dr. Timothy Stenzel: Yes, 80% at least for antigen tests, whether it's a central lab moderately complex or point of care or home. Specificity, we expect to be relative high, especially as the rates of infection go down. We don't want to have there to be too many false positives relative to the true positives. It would kind of defeat the purpose of the testing and, you know, have a lot of follow-up testing. It's just really confusing. Typically, we prefer not to see specificity any lower than say NPA lower than 98% but we do assess this on a case-by-case basis.

The other thing is, antigen tests for the moderate and high complexity environment, we are prioritizing high volume tests typically on automated instruments. This woman is wanting to take the lateral flow test and submit it for moderate or high complexity testing environment that's not a current priority. We would urge you if have a rapid test, then do the point of care studies. That's where it's needed other than a central one or at home.

Natalia: Okay. Thank you so much. Yes. And I believe we kind of, you touched on this before, but what do you consider a high throughput test? Is there any kind of a specification right now that you have in your mind or anything like that?

Dr. Timothy Stenzel: So, as with all things in the pandemic, this does remain somewhat flexible depending on the current public health needs. You know we are typically looking at full automatic systems for the kind of volumes that we're talking

about. But and we always recommend that if you need to know if you would qualify for our current thresholds, submit a pre-EUA just with that question. You know and you can add other things to the pre-EUA, but we need to know enough details about your method and the throughput and the steps that it would be able to assess whether it meets our thresholds for priority.

Natalia: Thank you very much.

Coordinator: Our next question is from Jackie Chen. Your line is open.

Jackie Chen: So, hi. I have a follow-up question on neutralizing antibody tests. The first question is you mentioned there is an International standard. Where do I find this International standard? I'm not aware of this? And the second question is, would a quantitative neutralizing antibody test that is completely automated and can test 20 tests at once be considered as a high throughput instrument and will it still have high priority. We did submit a clinical plan to FDA to try to get, to try to get guidance on how to do, on how to get effects testing for vaccinated populations.

And we are waiting for FDA's guidance before we begin the clinical study, in particular like we are willing to expand the sample size and also, the length of the study. But we just haven't heard from FDA for the pre-EUA yet so wondering what we can do to expedite that process? I know that's a long question. Thank you.

Dr. Timothy Stenzel: The International standard for serology is not, to my knowledge, a neutralizing antibody standard but it is, it was overseen by WHO. So, check with them. The FDA does not provide the reference material. It's for truly, it's for use to develop a truly quantitative test. You know I think the best of the neutralizing antibody tests do fully, will fully quantitate, the level of

neutralizing antibodies. And so, it's, I think it's possible to use the WHO standard to establish a truly quantitative test and then also, do the validations we recommend for a neutralizing antibody test.

And again, if you want to know if your test would qualify for a priority, then I would submit a pre-EUA and ask that specific question. If you haven't heard back from our team and it's been anything over a week or two, just and go back through and ask to copy Toby and me and we'll help check on that for you. Okay?

Jackie Chen: Okay. Thank you. It has been three weeks so I will update with further validation data and copy Toby and you. Thank you. And then there was one more question, the question that I asked was in particular about the validation requirement to get the vaccinated, to get the claims for immune protection. I guess the biggest thing we need to know before we can start our clinical study is the sample size and the length of the study. I'm just wondering if you have any opinion on this yet. If FDA has had any opinion on this yet?

Dr. Timothy Stenzel: So, I mean, from a scientific perspective the best way to do these studies is in correlation with a vaccine developer and maybe preferably with a vaccine developer that has an EUA-authorized vaccine and who is treating in the US. And the reason why that could be potentially a very good study design is we know exactly when the patient, if they were antibody negative, prior to entry into the study. We know exactly when they got exposed when they received the vaccine, and they have good timelines. You can look at antibody levels and you're also looking at the ability of those antibodies and those antibody levels to protect an individual from symptomatic and/or asymptomatic infection. So, you know, that's the kind of outcomes study that we believe will show a correlation with protection and herd immunity.

It's really hard to do it another way. Neutralizing antibody is only a surrogate for sort of immunities and certainly and the other thing, that's only in the B cell compartment. It doesn't have anything to do with the T cell compartment. So, you know, this is a complex area, and we haven't yet seen data at the FDA that allows us to assess what is an appropriate level of antibody and what it means. So, it's somewhat a little bit complicated to, I mean, we could probably say that certain designs of studies that aren't good. But it's a little bit hard to say what is needed, right, and to sign off on something that has never been shown or proven before.

So, however, we believe that antibody tests are very useful today and certainly the development of antibodies after vaccination, if properly assessed, using the right tests for the vaccine. I would urge everybody to read that communication that came out today. You know you can see whether antibodies were generated and it's just, you know difficult to know what that means at the present moment. All right. I think we'll, if there are additional questions, I think we want to move on to the next question. Thank you.

Coordinator: Our next question is from Don Caffiter. Your line is open.

Don Caffiter: Yes. Hello. Thank you for taking the call. Can you hear me?

Dr. Timothy Stenzel: Yes.

Don Caffiter: Okay. Good. We know that there have been a couple of EUAs authorized for sequencing COVID assays and we were wondering if there's a template under development for that? And if not, whether you can add any flavor in terms of what the FDA's expectations are other than the two EUAs that have been approved?

Dr. Timothy Stenzel: Yes. We haven't been inundated on sequencing applications. So, I don't know if it warrants a full template build out and go all through the clearance process for such a template but we're very open to submissions. Our team has developed some current recommendations that they can share with the developer if you're interested. And I would just reach out to through the template email address and ask for, you know, the recommendations for either sequencing validation or if it's not a full genome sequence, genotyping validation even if it gives a sequence technology. And there's different technologies that can assess individual say mutations as, you know, are probably quite a few that can be used.

Don Caffiter: Definitely.

Dr. Timothy Stenzel: We're doing the, we're providing these recommendations on a case-by-case basis rather than, you know, because at this time there hasn't been enough demand for the recommendations to spend time on a fully baked template.

Don Caffiter: Okay. So.

Toby Lowe: And if you do send in an email asking for, for discussion. If you could send additional information about your test, that's helpful. So, there are, you know, different approaches to sequencing tests. The recommendations are often specific to your situation.

Don Caffiter: Okay. Very good. Thank you to Tim and Toby. Thank you.

Coordinator: Our next question is from Franco Calderone. Your line is open.

Franco Calderone: Thank you, Toby, and team again. Okay. A couple of questions. One is related to the asymptomatic number of individuals that we need in order to get okay from FDA for then antigen test for at home use. Given that the prevalence is going down, thanks to increased vaccination. Do you anticipate modifying that requirement in any way, either pre- or post-EUA, that's number one. Number two I wanted to confirm on the cross-reactivity requirements in Part J of that template.

Our lab is assuming that we're, we're going to be working with inactivated pathogens, right? The list that you have there so that's the second part and the third part is the endogenous interference. Given that the lab what we are employing at is located in the UK. Some of these of these substances may or may not be available. Is there any flexibility in terms of what is the least number of these substances that need to be tested? And that's it.

Dr. Timothy Stenzel: Sure. I would reach out to, through the pre-EUA process, to ask about specific interference. We've clearly authorized some tests that hadn't completed the recommended list. They've got most of them, both on other pathogens, and potentially some interfering substances. However, that should be negotiated with the review team about on what could serve as the minimum that we recommend to do. But we do recommend doing the standard ones that we'd recommended in order to assess inactivated pathogens are typically fine. All of them aren't necessarily, you know, unsafe to work with.

So, they don't necessarily have to be inactivated some of them. You know those that are BSL level II or lower. The BSL III or above that, you know, obviously inactivated pathogens usually will be used in certainly otherwise, you have to have the capabilities to handle them which you do. And then as far as asymptomatic testing goes, so, and I think you were looking at a home test, is that correct?

Franco Calderone: Correct.

Dr. Timothy Stenzel: Yes. So, we have, you know, a fairly recent, a new amendment, for home tests that whereby, you know, prior to authorization developers don't have to test a single asymptomatic individual. They simply determine the performance in asymptomatic population with 30 positives. And if performance meets the amendments, you know, recommended levels then we can authorize that test for OTC. As long as all the other OTC recommendations other than testing asymptomatics are conducted and are acceptable. We can authorize that as an OTC test for screening if the developer agrees to a serial testing plan. So, that for managing tests, it would be two to three times a week and for a molecular test, that would be once a week.

So, I would urge you to check that, that recent amendment as you may find that helpful to get to the market as soon as possible. It's designed for that purpose. If a developer wants to take such a test as you have and wants to accumulate enough pre-marketing, asymptomatic patients. That they can and we would ask for a minimum of 10 asymptomatic positives that says the comparative test is positive on 10 asymptomatic's. And we can go ahead and authorized for single test use if performance is good enough and not require serial testing, not have to follow the serial testing plan. As the number of positives do decrease, unfortunately it's still quite a few in the United States.

But as it does decrease and continues to decrease hopefully, we are allowing enrichment strategies. You know this is not having to test every single person in the study in order to find the positive. But having a method to identify positives by another method, acceptable method and then pull them out and do the assessment on them. It's important, very important to run your enrichment plan by the FDA in the form of a pre-EUA submission. So, that we can assess

bias in the study plans. So, we've clearly seen examples of bias which were unacceptable and it's important. Such as, a patient shouldn't know the result of the comparator test prior to testing with a candidate device. That would be a no-no.'

So, hopefully you find that new amendment pathway useful because you don't need to do any asymptomatics pre-market. We do ask for a post-market commitment of confirming performance and your serial testing plan, i asymptomatic screening population.

Franco Calderone: Thank you very much. That was very nice.

Toby Lowe: And just to clarify it because I think you mentioned that you have antigen test. The supplemental EUA template is what Tim is referring to. There's also an EUA amendment for molecular tests that has a similar approach but for your situation, the supplemental EUA template would lay out the approach for your situation.

Franco Calderone: Got it. Thank you very much.

Irene Aihie: Thank you, Operator. I believe that was our last question. This is Irene Aihie and we do appreciate your participation and thoughtful questions during today's Town Hall. Today's presentation and transcript will be made available on the CDRH Web page at [www.fda.gov/training/cdrhlearn](http://www.fda.gov/training/cdrhlearn) by Tuesday, May 25. If you have additional questions about today's presentation, please email [cdrh-eua-templates@fda.hhs.gov](mailto:cdrh-eua-templates@fda.hhs.gov).

As we continue to hold these Virtual Town Halls, we would appreciate your feedback. Following the conclusion of today's Virtual Town Hall, please complete a short 13-question survey about your FDA CDRH Virtual Town

Hall experience. The survey can be found now at [www.fda.gov/cdrhwebinar](http://www.fda.gov/cdrhwebinar).  
Again, thank you for participating and this concludes today's Virtual Town  
Hall.

Coordinator: Thank you for participating in today's conference. All lines may disconnect at  
this time.

END