FDA Virtual Townhall

Moderator: Ivory Howard
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12:15 pm ET

Coordinator: Welcome and thank you very much for standing by. At this time, all participants are in a listen only mode. At the end of today's presentation, we will conduct a question-and-answer session. 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 Ivory Howard. You may begin.

Ivory Howard: Thank you. Hello. I'm Ivory Howard of CDRH's Office of Communication and Education. Welcome to FDA's 53rd webinar in a series of virtual Town Hall Meetings to answer technical questions about the development and validation of tests for COVID-19.

Today Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health and the Office of Product Evaluation and Quality, and Toby Lowe, both from CDRH, will provide a brief update.

Following opening remarks we will open the line for your questions. Please remember that during this Town Hall we're not able to respond to questions about specific submissions that might be under review.

Now please welcome Dr. Timothy Stenzel.

Timothy Stenzel: Hello and, you know, welcome again to this Town Hall call. And we look forward to helping as much as we can on this call.

And we do have some questions we received in our inbox. Last week, I neglected to go over those. My apologies, we'll try to hit all of those that we haven't already answered offline today.

I'll start off just by, you know, going over our current priorities again. They remain focused on expanding access to testing. This includes primarily diagnostic tests at home and point of care tests, and also collection at home and as well as extremely high throughput central lab tests.

And with that, I will turn it over to Toby who will have some additional announcements. And then we'll get into the questions that we received prior to the meeting. Thank you.

Toby Lowe: Thanks Tim. Thanks everyone again for joining us today. Just a quick update on the web page for EUA authorized serology test performance. If you're on our email list you likely got an email earlier today. That page has been updated to provide additional information on the expected predictive value of authorized serology tests that have submitted performance data to provide information for prevalence assumptions ranging from 5% to 50% to potentially help healthcare providers interpret those antibody test results for their patients in their communities.

And then I wanted to quickly update again on the pooling and serial testing amendment that went out last week that I believe (Chris) and Tim spoke about

on the Town Hall last week. There were a couple of topics that we wanted to highlight. I know that one of the topics that came up last week was regarding a condition of approval. I believe its Condition F about a post-authorization study.

And we just wanted to clarify. That commitment or that condition is specific to the screening aspect of the indication. So the pooling aspect we do expect to be validated ahead of time as outlined in the amendment.

And those - that validation should be submitted as part of your request to be added to the exhibit. The post-authorization condition lines up with the approach that we outlined in the serial screening supplemental template that we posted last month. March 16th I believe. That provided a path for authorization of screening claims prior to validation with asymptomatic individuals.

So under this amendment we've rolled that in so that if a test did not previously have screening claims the amendment will give that test the serial screening claims and the post-authorization condition requires that validation with asymptomatic individuals.

So we wanted to clarify that. And hopefully everything else was fairly clear on that amendment. But I think we do have some of the questions that we'll go through, also touch on that. So we'll talk some other aspects of it.

So moving onto the questions that were sent in ahead of today's call, actually the first one is about that pooling and serial testing amendment. And the - this question is specifically asking whether this only applies to RT-PCRs or whether other types of nucleus acid amplification tests could also fall under this amendment.

So the amendment is specific to previously authorized molecular-based RT-PCR SARS-CoV-2 tests that are - that meet all of the criteria outlined in the amendment. This is based on the experience we've had with SARS-CoV-2 tests over the past year and our experience with data that demonstrates that tests within the scope of the amendment are likely to maintain appropriate performance when they add pooling.

Other types of NAATs may be able to add the same indication but we would expect an individual supplemental EUA request to add the same pooled serial screening indications. The validation approaches that are outlined in the appendices of the amendment may be applicable depending on the technology. But you would have to take a look and see whether those validation approaches would work for your test. For example, there are, you know, some of the validation approaches require the use of CT scores and some tests don't return CT scores.

So there are two validation options for media pooling. Option 2, I believe it is, does not rely on CT scores so that would likely be the applicable validation option for a test that does not use CT scores.

Tim, did you want to add anything on that?

Tim Stenzel: No. I think that's good. Thanks Toby.

Toby Lowe: Okay, great. The next question is also about the pooling and serial testing amendment asking whether - this one is asking about that post-authorization study for asymptomatic and asking whether both analytical and clinical performance testing can be provided post-authorization. And then further asking about whether amendments to the - to an existing EUA would include

all instruments that are included in the existing authorization if they are eligible.

So to clarify again, the pooling and serial testing amendment is only applicable to previously authorized tests that meet the eligibility requirements as stated in the amendment. So this includes having specific performance criteria per specific validation and design specifications as authorized in the underlying EUA.

For example, a previously authorized test that was validated with contrived specimens or for which the PPA is less than 95% would not fall under this amendment. Similarly, a test that does not have multiple targets on SARS-CoV-2 genome or a multi-analyte test would also not fall under this amendment.

For tests that do meet the criteria for the amendment the test configuration as authorized would be amended. So if that includes multiple instruments that would carry through in the amendment.

And then for the question about validation the amendment letter includes multiple appendices for different indications and different validation options. So those appendices include the validation requirements to meet the conditions of the amendment.

And I know that, you know a lot of times we talk about our validation recommendations or expectations which is, you know, sort of what we refer to as guidance language. The amendment is different. These are requirements. These are specific metrics that must be met in order to qualify under the amendment.

So the amendment spells out those requirements and it outlines a process for an EUA holder to submit the required validation for the indication that they're requesting. And the expectation is that that pooling validation as outlined in the applicable appendix is submitted along with the request to be added to the exhibit for the amendment. And that would be for anything pooling over an N of 3 as the amendment does provide for pooling up to and equal 3 without additional pooling validation.

And that request for it to be added to the exhibit of the amendment would include, in addition to that validation data, would also include the other information that's outlined in the amendment such as the pooling procedures and the updated labeling.

And that all needs to be submitted prior to the test being offered for an indication under the amendment.

And then we did talk already about the post-authorization condition that is for the asymptomatic screening claim.

All right, so the next question we have is also about pooling and partially about the same amendment and partially separate. So this is asking about pooling without preauthorization from FDA and whether that's limited to pools of three.

So to clarify, the pooling and serial testing amendment is not quite pooling without preauthorization. For pooling up to three we don't ask for any additional validations when the other requirements of the amendment are met. But the request under the amendment does need to be submitted to FDA prior to a test being offered for that indication.

And the question is also asking about different specimen types including saliva. The amendment is limited to anterior nasal swab specimens. And the indications are for pooled testing of asymptomatic individuals tested at least weekly as part of a Serial Testing Program. This question is asking also about testing pooled specimens outside of Serial Testing Programs.

So that would not fall under this amendment. The validation requirements are for that pooled serial screening. The anterior nasal swab is - are laid out in the appendices of the amendment and should be submitted ahead of testing.

If a sponsor is interested in offering pooled testing separate from a Serial Testing Program or offering pooled testing with specimen types other than anterior nasal swabs you can submit a supplemental EUA request to your underlying EUA to request those claims.

For pooling of anterior nasal swabs separate from a Serial Testing Program you can consider the same validation approaches that are in the appendices of the amendment. However, since we have not yet authorized saliva pooling and we have in some cases seen data for saliva pooling that does not look promising, we do continue to recommend the validation as outlined in the EUA template.

And if you have alternate approaches that you'd like to discuss you can reach out with questions or submit a pre-EUA.

Okay. The next question we have is also about this amendment. And it's asking about whether physician authorization is required. So to clarify, the pooling and serial testing amendment does not change the prescription status of the previously authorized EUA. This question is also asking about whether CMS could do anything about making a CLIA Waiver not required.

You know, we would suggest that you reach out directly to CMS about any questions related to CLIA requirements. Our understanding that we've discussed on this call before is that a CLIA certificate is needed any time a test is performed by a facility and that self-testing using a test authorized for home use would not require a CLIA certificate.

All right, I think we are moving onto questions not about that template now or sorry, not about the amendment. There is a question about the sensitivity of rapid tests for variants.

And at this time we don't have any reason for concern regarding the sensitivity of currently authorized rapid COVID-19 tests. And we are still monitoring the impact of viral mutations on COVID-19 tests. And we do have the new SARS-CoV-2 viral mutations web page that we put out last month, I think, that we will update when additional information becomes available.

We have a question about molecular tests validating for point of care and the ability to use banked samples if 30 symptomatic positive samples are not achieved after 2 weeks of enrollment whether they can be supplemented with banked sample. They're asking whether some negative banked samples should also be tested and if the banked samples need to come from symptomatic subjects or if they can be from any positive or negative samples.

So this will depend a little bit on the indication that you're looking for. To support a screening claim we do recommend that negative specimens come from the intended use population so asymptomatic individuals. To support a suspected of COVID claim or symptomatic claim we have accepted

specimens from both asymptomatic and symptomatic individuals since both populations can be considered suspected of COVID-19.

And then the follow-up question there is regarding whether the banked samples or if banked samples are used to supplement, do they need to be the same sample type as what is claimed in the IFU? For example, if the sample type claimed is direct samples with no transport media but the banked samples are in transport media, is that acceptable?

We would expect that the banked samples should be the same sample type that you intend to claim for your device. So if you are claiming a direct swab for your test then we would want to see direct swabs used in the clinical validation study.

Our next question is about preparing a 510(k) for a molecular SARS-CoV-2 test and whether - and using BioFire as a paper predicate but clinical data from an EUA asking about whether we - whether FDA expects to see precision and reproducibility studies from a minimum of three sites and whether one site can be the manufacturer site.

So that is correct that BioFire is the only available legally marketed predicate at this time. We do understand that it may not be feasible to use BioFire as the comparator for your clinical study. So you may use an EUA authorized high-sensitivity RT-PCR assay as your comparator.

And to support a 510(k) a reproducibility study is expected. Your reproducibility study should include different sites in order to evaluate reproducibility across sites and different operators in order to evaluate reproducibility across operators.

So we would generally expect three or more sites with multiple operators at each site. And if the manufacturer site has an appropriate lab that can be one of those sites.

And I think we've mentioned previously on the call that if you're pursuing a 510(k) we do suggest that you submit a pre-submission to discuss your proposed validation strategies and comparator methods for review.

So I think at this point, why don't we switch over to live questions? And we can jump back to some of the other pre-sent questions a little later in the call.

Coordinator: And at this time, 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 it looks like our first question is from (Senko Calderon). Your line is open.

(Senko Calderon): Thank you for taking my call again today. So I have an article, a Wall Street Journal article in front of me. At Home COVID-19 Test might cost too much for regular use. And the article is from today referring to BinaxNOW on the Quidel QuickVue, which as many of us know have been shipped to pharmacies to be available for over-the-counter purchase and self-use.

The article criticizes the price. I mean I'm not here to talk about it. I don't expect - I'm here to talk a little bit about the frustration that we have been going through. It's been about eight months that we, you know, we started this process.

And the biggest issue we have encountered is not related to the clinical performance of our rapid tests, which are just the naked strips, as we call them, exactly like the QuickVue.

But it's related to the analytical requirements because these are - these have to be done in a BSL-3 facility. So we thought we had a solution for this. We had contracted with a company that was going to do this. And as it turns out, they are not going to be able to do. So we're back to square one.

So we have supply. We have the tests. We have the performance. Yet we cannot pass this hurdle.

Now if we talk about countries like Germany and the UK for instance, in the UK, Porton Down Street, you know, you can send your tests there. They validate them for you and then they make them available to folks. Germany does the same through BfArM and the Paul Ehrlich Institute.

And what you see in those two countries is that you have dozens of antigen tests available for, you know, in the EU for about 2 or 3 Euros a piece now. You can buy them in any pharmacy.

So this is not a criticism to FDA but rather a question. Do - is it realistic to think that FDA may adopt some of those practices, you know, similar to what's going on in the UK and Germany or the EU in general where the availability of these tests is massive now, you know?

And then the final question is coming back to the analytical part. Would FDA be amendable to accepting studies let's say from an institute like Karolinska in

Sweden given that we've had a very difficult time finding the BSL-3 facility that can conduct those studies on our behalf?

Finally, is it possible, and this has to do with the comparator test. We feel comfortable about the clinical validation in our small studies.

But does it make sense to use a high-performance RT-PCR test as a comparator test with CT values rather than let's say the Abbott BinaxNOW or the QuickVue which are, you know, in our case are exactly the kind of tests that we're going to be bringing to folks? In fact the QuickVue is exactly like our test. I end my long comments and questions there.

Timothy Stenzel: Yes. Yes. You know you bring up a number of important topics. We typically ask one - you know have callers ask one question.

(Senko Calderon): I'm sorry.

Timothy Stenzel: First of all, we'll look at all available data that a sponsor, a test developer wants to submit to the FDA. You can contract for any of the work with anyone you want as long as it's done well. And, you know, if it's not according to our recommendations we urge you to check with us first through a pre-EUA submission.

You know you actually aren't required to use things that require a BSL - you aren't required to do testing that would require a BSL-3 lab. There are different ways to do that. And, you know, I'd reach out directly to the FDA and with the specific questions you have about that.

But there are many different ways to address that. And one of them, you know, is to use inactivated virus. Either heat or radiated virus is a good

substitute as long as your test isn't impacted by inactivation, that there's flexibilities around using actual clinical samples and diluting them down for analytical studies.

So there is no requirement by the FDA to use - to do testing that requires a BSL-3 level lab. So just reach out to us through our template email address or through a pre-EUA to address any of those.

The U.S. does - we do speak with our international colleagues on a regular basis. And we're familiar with what they do in other countries. And we exchange information all the time.

And so we look at what they do and they look at what we do. And sometimes we depend on one another for important information. And that's an ongoing effort. In fact, I have another call tomorrow morning.

And then as far as the comparator test, what we're trying to establish with the comparator test is truth. And so we are looking for high-sensitivity molecular tests. For antigen direct tests, you know we're looking at performance within the first five to seven days of symptoms and longer if your tests prolongs well over longer periods of time after initiation of symptoms as some of the antigen tests that we've authorized have demonstrated.

So we're looking at truth in those first symptomatic days. And that's important so we'll be adhering to that recommendation.

If you have - we're always open to alternatives. But, you know, that's what our scientists say is the best thing to do right now.

And let's see. The other thing is, you know, we don't tell commercial test developer what they can or can't charge for a test. The FDA is not involved with that.

But both the tests you mentioned can be produced in extremely high volumes and the U.S. Government has funded both those companies along with many other companies to both develop tests, launch tests, and greatly expand the manufacturing capability of those tests.

And so that's something, you know, that I think the U.S. Government is doing a pretty good job with. And is always looking, I think, for opportunities to further expand access to testing.

So with that, I think I'll want to move onto the next caller.

(Senko Calderon): Thank you for that.

Coordinator: Thank you. And our next question is from (Koto Modivenka). Your line is open.

(Koto Modivenka): Good afternoon. Thanks for taking my call. I think in the beginning of the - today's thing, Toby mentioned something about the serology testing from 5% to 50%. I missed what she mentioned. Can you please repeat and explain what you mentioned please?

Timothy Stenzel: Toby, over to you.

Toby Lowe: Sure. Yes, sorry. I was having trouble getting off mute there. So the - we have a web page on the EUA authorized serology test performance. And that web page was updated this morning to provide additional information on the

expected predictive value of authorized serology tests when there are prevalence assumptions ranging from 5% to 50%.

(Koto Modivenka): Okay, thank you.

Timothy Stenzel: And yes. It should be live so you can go and take a look at that. And see if it is helpful.

Toby, why don't we go back to the next question that was submitted ahead of the call?

Toby Lowe: Sure, absolutely. Let's see. So the next question that we have is about antigen tests. And this question is stating that, you know, based on the tests that we've authorized that sensitivity is not more than 80% with specificity often close to or above 98%.

And asking - stating that the sensitivity is often determined with a panel of 50 to 80 high positive PCR samples. So first we want to clarify that all antigen tests are validated with data sets that include 10% to 20% of low positive specimens.

So the - so it's not quite accurate to say that the sensitivity is established with - only with high positive PCR specimens. They do include low positives.

And additionally, the results from antigen tests are presumptive negatives. So the rest of this question is asking about using these tests with lower sensitivity to make decisions about reducing social and safety behaviors like social distancing.

And so we - you know the labeling for the antigen test does indicate that these are presumptive negatives and should not be used to make determinations about isolation or social distancing practices. And further that if it's necessary for clinical management the tests results should be confirmed with a molecular assay.

Timothy Stenzel: And, you know, just add -- thank you Toby, that -- you know, point of care and rapid tests and especially antigen tests are less sensitive than central lab molecular, high-sensitive molecular tests.

And however, in order to really expand the reach of testing, you know, rapid tests, lateral flow tests that can be performed simply at the point of care, be cost efficient, and be available at home for home testing as we've authorized. You know the - maintaining the same performance expectations and recommendations as a central lab molecular test would really, you know, not allow these tests to really add to the fight here against COVID.

And Toby's absolutely correct in talking about negatives in these tests that are below 95% PPA or sensitivity, are presumed negative. That's standard labeling language that we authorize.

And in addition, we really strongly support serial testing of not just these rapid point of care and home lateral flow tests but really of all tests if we want to do our best as a laboratory and healthcare community at capturing and identifying asymptomatic individuals.

Okay. I think, Operator, we can go back to the next live question if there is one. And we can somewhat alternate going to and fro.

Coordinator: Sure. Our next question is from (Savannah Estes). Your line is open.

(Savannah Estes): Thank you for the updates today. This is (Savannah Estes) from UserWise Consulting. My question is regarding usability testing for instructions for use for an over-the-counter molecular test.

So if a manufacturer intends to provide instructions in two different languages in one combined digital IFU, for example, if the instructions were provided in both English and Chinese, would the FDA expect to see usability testing with Chinese speaking users?

Timothy Stenzel: Toby may know the answer here. I know that our recommendations are English and Spanish in the U.S. for OTC. And certainly developers can add additional language.

Toby, do you have - I forget about usability in non-English languages. Do you remember?

Toby Lowe: I'm not sure. If you can send that question in, we can try and get you a response.

(Savannah Estes): Okay. That sounds good. I did realize that Spanish is called out specifically in the templates. And I've read that if the languages are provided in separate documents, it may not be required to have Spanish speaking users included in testing.

So I guess with that assumption, does that change your thought process at all if the documents were to be combined or separated?

Timothy Stenzel: Yes. I mean we go by what's in the template as far as our recommendations are concerned. I think that's a great question to send in as Toby recommended.

(Savannah Estes): Okay.

Timothy Stenzel: And we'll take a look at, you know, whether we update the template and make it more flexible, which is always our goal is to constantly review what we do and see how we can improve our recommendations.

(Savannah Estes): Okay. Yes. We definitely appreciate that. Thank you.

Timothy Stenzel: Okay. Toby, why don't we go back to the next question submitted ahead of time?

Toby Lowe: Great. So the next question we have is regarding isolation or purification kits and/or extraction kits. And this is from a developer working to develop a new extraction kit to be used with existing third party PCR assays in high complexity labs.

So generally we would recommend that you work with a test developer. The - generally assays that we authorize under EUA specify the extraction reagents with which the test has been validated and with which the test has been authorized.

So if you're developing a new extraction kit those are generally Class 1 exempt devices and can be marketed under the Pro Code JJH. And so you - we would recommend that you develop your device under a 21 CFR Part 820 compliant quality system. And then you can register and list your device under the JJH Pro Code and collaborate with test developers of authorized

assays that may be interested in validating their test with your extraction kit. And then those assay developers could submit a supplemental EUA request to add your extraction kit to their authorization.

Timothy Stenzel: Okay thank you Toby. I'll go onto the next question submitted ahead of time. And this has to do with breath test development. You know breathing into some sort of device in order to potentially detect SARS-CoV-2.

You know we have prepared our current thinking for this type of test development. And anyone who's interested in that I would recommend that you ask for those current thoughts for - through our template's email address and our team will provide our current thinking. We are providing - we are preparing a template for the breath test.

And we don't know when that can be publicly available. But we do have current drafted thinking and we can share that with you.

There's a specific question about our recommendations around the fact that we do believe that breath tests should - we recommend targeting the asymptomatic population as we think the benefit/risk ratio works best in that situation.

And the question had to do with how can one enrich a population to it to make this easier to accumulate the asymptomatic positives?

We're open to enrichment at the - I would ask that you submit a pre-EUA with the study design. And then we can discuss that with you.

Our current thinking also provides sort of the number of positives and the number of negatives that we'd like to see in the validation study for these

devices. And if you send an email to the template email address we'll respond with those as well.

Okay, Operator with that, we can go back to any live questions.

Coordinator: Sure. And at this time, I would like to remind participants if you would like to ask a question over the phone line to please press star 1. Please be sure to record your first and last name clearly when prompted.

Our next question is from (Eric Penny). Your line is open.

(Eric Penny): Hi. Thanks for taking my call. Considering the acknowledgement that certain variants affect certain treatments, will there be any clinical utility for a companion diagnostic test to identify the KLA variant or specific mutations involved with a positive specimen?

Timothy Stenzel: Can you repeat that question? And then also address what particular technology you want me to respond about, serology, antigen, or molecular.

(Eric Penny): Sure. So this is specific to identifying variants no matter what the means is whether it's sequencing or an array or other.

But the question is considering the acknowledgement that certain variants affect certain treatments will there be any clinical utility for a companion diagnostic test to identify either the KLA variant or the specific mutations involved with a positive specimen?

Timothy Stenzel: Yes. So right now we are in discussion with a number of test developers both sequencing-based and genotyping-based to bring forward assays where either one of two situations can occur. The first is that the test developer may want

to be able to report the genotype or variant or mutation information to the clinician and/or the patient and from the lab.

And we're open to that. And we now have prepared recommendations for the validation of such sequencing or genotyping test. So developers can email our template email address and ask for those current - that current thinking.

And then there is another pathway that is open. And that is that for test developers who develop a test that both detect SARS-CoV-2 and also genotype or sequence but they, you know, are not wanting to go forward with having those genotype or sequence data reported to clinicians or patients but there is a public health need to - for public health authorities to see that information.

So if reporting is only to a public health authority and not to the clinician or patients where the FDA is not going to regulate that genotype or sequencing component of that SARS-CoV-2 detection test.

So we would - the FDA would review SARS-CoV-2 detection. And we would make sure that the labeling is appropriate that the genotyping or variant or sequencing information is not transmitted to patients unless validated and authorized by the FDA.

You're talking about an extension beyond that and any correlation with specific therapeutics or vaccine. We have not gotten that far in our thinking. I would - always interested in studies and data that show that that's - really has a clinical impact. And, you know, I'm sure at some point it definitely will.

So I mean if you have data, publications that, you know, we haven't seen, you can always make sure and forward that to our template's email address and it'll be distributed. We are trying to keep an eye on everything. But we don't necessarily catch everything.

And if you have a specific test in development where you would like to make certain claims, you know, submit a pre-EUA and include the information that you think is important. And we'll give you feedback on that.

So hopefully that - well as helpful as I can be today. And hopefully that's somewhat helpful.

(Eric Penny): Yes. That was very helpful. And we actually have a full set of both analytical and clinical evaluations for all known variants to date. So we should just go through the pre-submission process with templates. Correct.

Timothy Stenzel: If you've already done all the data collection and you - or if you haven't completed all your studies, if you haven't completed all your studies then immediately send in. As soon as you can, send in a pre-EUA. If you've completed all the studies and you want us to review it for an EUA authorization just, you know, submit that.

But we're very happy to give feedback through a pre-EUA for any studies you haven't initiated yet.

(Eric Penny): Perfect. Thank you very much.

Timothy Stenzel: Operator, let's take another question, please.

Coordinator: And at this moment, I'm showing no further questions.

Timothy Stenzel: Okay. Toby, do you want to go back to the questions that were submitted ahead of the call?

Toby Lowe: Absolutely. We just have a couple left here. So the next one is about a quantitative test for antigens or SARS-CoV-2 antigen tests and asking about comparison between quantitative values between different antigen tests, so we do want to clarify that we do not currently have any EUA authorized quantitative COVID-19 antigen tests. The authorized devices do establish the assay's limit of detection. And they do use different measurements between different tests that are not comparable.

So until we have a fully quantitative antigen test or establish reference material, we're not able to evaluate the direct comparisons of the performance and correlation of the quantitative value between those antigen tests.

And the last question that we have is about FDA's position on a finger stick point of care serology test that uses a full S1 protein antigen and whether if all performance and other criteria in the current serology template is included, does this help address FDA's concerns on current variants that are occurring in the U.S.?

So first, we do currently prioritize review of EUA tests where authorization would increase testing accessibility which would include serology tests intended for use at point of care settings. And that's regardless of the antigens used in the assays to capture the antibodies against SARS-CoV-2.

And regarding the concerns about variants we do believe that adequate performance demonstrated in the validation studies is important to establish the performance of the test but it would not necessarily address the concerns

regarding the potential impact of current or future variants on assay performance.

The serology template does include recommendations to provide a plan for monitoring new and emerging SARS-CoV-2 viral mutations and variants on an ongoing basis and for assessing the impact of mutations and variants that have been identified as prevalent or clinically significant on the performance of your assay over time.

So we would recommend that you take a look at those recommendations in the template as you prepare your EUA request. That is the last one.

Timothy Stenzel: Toby, I think that ends the questions that were submitted beforehand, if that's correct Toby.

Toby Lowe: That is correct.

Timothy Stenzel: And Operator, if there's any other live questions, we can take those now.

Coordinator: Yes. We had a question from - I wasn't able to understand the first name but it was (Gabrielle). Your line is open.

(Gabrielle): Hi. My question is regarding the tests developers making an asymptomatic claim. Given the low prevalence of SARS-CoV-2 in the U.S. at the moment and having it be difficult to get positive test subjects, and having the FDA asking for a minimum of 100 SARS-CoV-2 positive asymptomatic subjects, would it be acceptable to add to the validation test subjects from out of the U.S.?

Timothy Stenzel: What type of test is this again?

(Gabrielle): Breath test.

Timothy Stenzel: I'm sorry, what?

(Gabrielle): Breath test.

Toby Lowe: Tim, this is asking about breath.

Timothy Stenzel: Oh breath test.

Toby Lowe: Breath test, the same.

Timothy Stenzel: Okay. Okay.

Toby Lowe: It's similar to what you addressed a little bit earlier from the written questions.

Timothy Stenzel: Oh okay. Yes, the breath test, so we do not know the performance of this new kind of technology. We really don't - for respiratory disease. The FDA doesn't have any experience with this.

And so in order for us to authorize a brand new technology like this at least in the beginning until we get and demonstrate that it performs as well as more classical tests, we really do need to see that 100 asymptomatic positives, I think is what our current thinking is.

We are open to, as I mentioned earlier in addressing a similar question, we're open to enrichment technology or methods. We want to eliminate bias. So if you want to discuss that I would come in and speak and through our

template's email address either as a pre-EUA or a question about whether enrichment can be used for those tests.

We are open to studies outside the U.S. as well. It does depend on what setting you want this test to be validated and authorized for. But typically this would be a point of care test and/or it can be even an over-the-counter test or a home test. In those situations such as point of care and in the home, we ideally would like to see U.S. home users used. That can be either in their home or it could be in a simulated home environment that a test developer sets up in any facility they want.

So some of these breath tests are not necessarily able to be used at point of care at home due to the equipment requirements, and then it may be limited to more of a moderate or high complexity lab setting. And we may be - it may be easier to show performance in the intended place of use if it's a moderately to high complexity test.

So I would come in and ask those specific questions to the FDA. And we'll do our best to ease, you know, the path to demonstrate performance of your breath test.

(Gabrielle): Thank you. Because it seems that asking 100 positive asymptomatic and then having about 30% of all positives being asymptomatic and having an all comers approach, I mean that would - having the prevalence in the U.S. about 2% and the ability to ask about 50,000 test subjects. Is that correct?

Timothy Stenzel: Well, I can't do the math right now. And prevalence is variable within the U.S. And that's why absolutely we are open to any sort of enrichment process. And, you know, in the past some of these processes could be connecting up with a Serial Testing Program for schools or workplaces or

convalescent centers where the catchment is rather large and you can enrich your population that way.

You know one of the challenges with this technology is we're really trying to tell how sensitive and specific it is for a virus and not the actual molecules that technologies are developing - are detecting. You know the analytical detection of those molecules can be proven very easily.

But, you know, the implications for clinical diagnosis or screening, you know, haven't been demonstrated.

All right, I don't know if there's another caller or if we have time. I think we have to move on.

Coordinator: Yes. I'm currently showing three questions in the queue. Did you want me to take another question at this moment?

Ivory Howard: Yes. We'll take one more call.

Coordinator: Sure. Our next question is from (Susan Sheldon). Your line is open.

(Susan Sheldon): Hi guys. Thanks for taking my question. I actually wanted to because I did send in an email. But I'll ask the question. There are - I have a - I'm developing a saliva test, also a nasal swab for all-comers as an over-the-counter test.

And on comparators I'm trying to devise this clinical trial and the comparators. I'm looking at a - because I know you have to match the sample kind with the testing of the PCR as the comparator. And I'm looking at the things that you have approved under Emergency Use Authorizations. And the

only thing I see that - with the high-sensitivity is in RT isothermal application. Is that acceptable because it's not RT-PCR per se?

Timothy Stenzel: I think you're asking what is the appropriate comparator for your test, which I'm not sure if it's antigen or molecular, probably molecular.

(Susan Sheldon): It's an antigen. It's an antigen detection…

Timothy Stenzel: Antigen.

(Susan Sheldon): …test. It's lateral flow.

Timothy Stenzel: Yes. For a comparator test and swab for saliva, that doesn't matter whether it's antigen or molecular. We are still recommending a nasal pharyngeal swab. And using a EUA…

(Susan Sheldon): Yes.

Timothy Stenzel: …authorized high-sensitivity molecular test. We do look for…

(Susan Sheldon): Right but…

Timothy Stenzel: We do look for cycle threshold numbers that are in the lower viral load level to make sure that we know the test performs across the dynamic range. And so you can use a test that doesn't have cycle threshold follow-up.

But then we really need to know another test, you know, what the cycle - using another test, what the cycle threshold is. So it's just probably easier to see a comparator test.

I'm not sure if I addressed your question though, so I'll let you ask a…

(Susan Sheldon): So in the template the comparator is described as an RT-PCR, that its high-sensitivity and it uses the chemical lysis extraction. It clearly defines what it is.

And when I'm looking in here for the swab specimens, I don't find a comparator that matches all those criteria. I find one that's acceptable but it says RT isothermal amplification. That's what I'm asking, is that acceptable?

Timothy Stenzel: Okay, all right. Well, yes, I think if you reach out to the template's email address. We'll work with you on what an appropriate comparator is for your test and your study.

(Susan Sheldon): Great, great. That would be awesome. Thank you.

Timothy Stenzel: We actually prefer that developers reach out and just double check the comparator they would use so hopefully that…

(Susan Sheldon): Yes. I will do that. Thank you very much.

Timothy Stenzel: Okay. And the other two callers who didn't get in, if they wouldn't mind sending an email to the email address for questions to be received in advance of the call, we can address those on the next call. Thank you.

Timothy Stenzel: This is Ivory your...

Ivory Howard: Okay, thanks.

Timothy Stenzel: Go ahead.

Ivory Howard: I was just going to say thank you. This is Ivory Howard. We appreciate your participation and thoughtful questions during today's Town Hall. Today's presentation and transcript will be available on CDRH Learn web page at www.fda.gov/training/cdrhlearn by Friday, May 7. If you have additional questions about today's presentation, please email cdrh-eua-templates@fda.hhs.gov.

As we continue to hold virtual Town Halls, we would appreciate your feedback. Following the conclusion of this webinar, please complete a short 13 question survey about your experience. The survey can be found now in the chat box or at 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