FDA Virtual Town Hall Series – Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests

Moderator: Irene Aihie
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Coordinator: Welcome and thank you for standing by. At this time all participants are in a listen-only mode. During the Q&A session, if you'd like to ask a question you may press star 1 on your phone. Today's call is being recorded. If you have any objections you may disconnect at this time. I'd like to turn the call over to Ms. Irene Aihie. You may begin.

Irene Aihie: Thank you. Hello. I am Irene Aihie of CDRH's Office of Communications and Education. Welcome to the FDA's 47th 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 In Vitro Diagnostics and Radiological Health, and Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality, 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 this 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. Thanks everyone, for joining today. I have a couple of updates and then I will hand it over to Tim for some more. First, I wanted to make sure everyone was aware that just this morning the updated templates on our Web site, we updated the serology template for test developers. And in that update we added some information about viral mutations and variants, and also did some clarifying edits throughout. So hopefully that will be useful.

And then we also posted a new template for test developers of serology tests that the text will correlate to neutralizing antibodies. So I know we've had a lot of interest in that template and a lot of people waiting for it. So it has been posted and we hope that is still helpful for you.

The other update that I have is that starting tomorrow we will open up the ability for you to send questions by email ahead of time for us to consider prior to the town hall, so that we can try and address potentially more frequently asked questions. So we will be - there will be an email that goes out likely tomorrow, with instructions on how to do that. And the email address will be CDRHWebinars@FDA.HHS.gov. But again, you'll get an email - if you're on the town hall email list you'll get an email with those instructions tomorrow, once that opens up.

And with that, I will turn over to Tim, to give some additional updates.

Dr. Timothy Stenzel: Thank you, Toby and welcome again, today. I am hearing that some callers may be having trouble calling in. So if our technical team could check on that and assist those callers, that would be great. Let me start off with, prior to getting to the main topic, with frequently asked question that we get about the use of frozen bank samples for validation of point of care tests on a particular antigen test.

And yes, we are allowing banked frozen samples to be used and banked samples can be mixed in with fresh samples. We still are asking that at least 10% to 20% of the positives are composed of low positive samples which reflect the natural distribution of SARS-CoV-2 viral loads. We have seen that even early in symptomatic disease that CTs can be relatively high.

Per the antigen template, you know, we do want to see these low positives, at least 10%. You know, and then we do want to see fresh sample as well, a minimum of five positive samples pre-market. And this is because we have noted multiple times now, both for molecular and for antigen, that freezing can actually for still specifically undetermined reasons, allows a greater sensitivity.

And so pre-frost studies can show that the performance is same or different. But just to be safe we do want to see a minimum of five fresh samples pre-market, positive samples. And then we would ask you to fulfill that on the rest of the samples being fresh after authorization.

Okay. With that, I will move into the main topic. So yesterday we issued a new policy, serial screening and particularly screening asymptomatic individuals which we view as a critical part of reducing the spread of COVID-19. You know, screening involves testing asymptomatic individuals who do not have known or suspected exposure to COVID-19 in order to make

individual patient decisions such as whether an individual participates in an activity based on the test results.

Yesterday we also issued a fact sheet to assist schools, workplaces, communities and others, looking to establish blood testing programs to screen asymptomatic individuals as they are selecting a test for screening. We also posted a new template for molecular and antigen tests for serial screening.

We expect that the recommendations and information we provided here for test developers, will help streamline the path to an EUA authorization for screening tests, specifically the template outlines, outline situations in which FDA may authorize certain tests for screening, with serial testing prior to conducting - prior to the developers conducting certain performance evaluations with asymptomatic individuals.

This may include, in certain circumstances, authorizing a point of care and at home tests for OTC, nonprescription use, if all the appropriate studies have been other studies for usability and user studies and user comprehension have been outperformed. In this situation we are leveraging evidence of a test strong performance in symptomatic patients.

Combined with serial testing it mitigates the risk of false results when testing asymptomatic individuals for the cases in which we have not reviewed the asymptomatic testing performance pre-market. And we expect to see that in the post market studies showing and demonstrating adequate performance in the post-market setting would demonstrate that adequate performance with the serial testing plan.

I want to back up a little bit, talk about how important home tests, point of care tests in particular antigen tests are. So starting in January 2020 we - the

FDA and other US government entities reached out to companies that are capable of producing antigen point of care tests and ultimately obviously, home tests which we've authorized.

You know, it wasn't that long to the year that we authorized our first antigen test. And then to date I think we've authorized 15 antigen tests. We are very interested in home use and on July 29, 2020 we issued a template with our recommendations, for home validations so that we can authorize both prescription and over the counter testing.

In September of 2020 in a piece on the Hill, we suggested that for a test that may be performing lower than recommended levels could use serial testing to improve overall performance using the combined results, two or more tests, to be able to achieve, you know, a good level of sensitivity. To date though, we've received no formal EUA submission of a fixed serial testing plan showing that it is functioning.

We hope this - that this new pathway, this new policy will accelerate the use of serial testing to reopen schools and reopen workplaces and other situations and say to keep convalescent settings safe. We recently were - FDA was recently briefed on a very well-designed, well-executed study that used serial testing of an EUA authorized molecular test and an EUA authorized antigen test.

And although it clearly showed that on a head to head competition or comparison, the antigen testing was significantly less sensitive than the molecular test. It also demonstrated that a serial testing program for the antigen test significantly mitigated the risk of false negatives in that serial testing program. So that was sort of the first really firm good evidence that we had and helped usher in this new policy.

So throughout this - throughout the year, last year, we have striven to provide flexibility and adaptability in approaches to validate all tests including home tests, screening tests. So we have authorized a number of screening tests, I think almost a score, and we hope that this greatly accelerates that as well. I wanted to go into a few more details.

You know, CLIA requirements are overseen by CMS and FDA's actions in this policy are not removing any CLIA requirements for the use of at home tests for self-testing in the - is not subject to CLIA requirements. This new template is also not automatically changing any authorizations. It is providing a streamlined path for test developers seeking serial screening claims.

So in order for a test to be authorized for OTC or nonprescription use, such tests need to be - needs to have previously shown asymptomatic screening data. But with this, since - in order to be an OTC test. But now we are allowing that data for asymptomatic performance using screening, to be revealed to us after authorization.

This template provides an option for screening authorization prior to collecting data or submitting - completing the validation for asymptomatic individuals. We would still expect validation symptomatic individuals as well as usability, user comprehension and layperson appropriate labeling for an OTC test.

For a developer who's already submitting that information, they would not need to submit more for FDA to authorize their test for OTC though. They can simply come in with a supplemented amendment application asking to convert to OTC based on the serial testing program.

Of course, the older pathway still exists. If someone comes in with, you know, meeting your performance expectations for an OTC test, on a one time test performance we will continue to authorize that, without the recommendation for serial testing. And that may be still an attractive option. Obviously we've already authorized many OTC collection kits and some OTC home tests.

So - and of course, providers must still order tests that are authorized only for diagnostic purposes and we're not going to object to the off label prescription use of those tests that don't have a screening claim. You know, the FDA does not determine the claims the test developer decides to request for their test or their application.

We are encouraging them to pursue this option if it's applicable to them and they are interested in it. We do authorize tests for certain indications and for certain - use in certain settings as appropriate by their validation. Generally point of care tests are authorized for use in the settings of under CLIA certificate of waiver with healthcare workers that are untrained non-laboratorians.

These tests typically included an instrument and required a trained user to operate them, but not always. And it's not required to have an instrument. CMS is responsible for oversight of CLIA certification. Of course tests that are authorized for at home use are appropriate for self-testing. Without a trained operator it may be used for self-testing at home or self-testing in other settings, such as schools, workplaces, and are not subject to CLIA requirements in that specific narrow self-test category.

Going further, each authorization indicates whether a test is for prescription or nonprescription use. Or as we said before in reiterating the fact sheet, when

we issued yesterday, tests authorized for a symptomatic claim, can be ordered by a provider for screening purposes and I've made that clear earlier in this discussion.

Some entities may use a blanket prescription to cover screening tests for their entire population. And if a test is authorized for OTC, over the counter, no prescription of course, is required. And as we've said previously including our prior FAQ and reiterated in the fact sheet we issued yesterday, you know, clinicians can absolutely order tests for off label use of screening. We're not going to object to that.

It is important however to be aware that certain tests include labeling. And state the tests should only be used for symptomatic individuals. These tests should not be used for screening and they would - this pathway would not be open to them. However, we do know that some groups are setting up testing programs for back to school, back to work, and prefer to use a test that is authorized for screening. That's an important point.

We have definitely heard resistance about using tests off label from some quarters and from some clinicians. And this hopefully paves the way for getting rid of that as an issue. And once we authorize a test for screening they of course are covered by PrEP Act coverage. So again, we hope that this streamlined path will lead to more test developers seeking and receiving a screening claim.

And as we indicated, and this is primarily for antigen tests that will be severely tested multiple times a week, we expect to see a minimum performance sensitivity for symptomatic testing of at least 80% with 70% as the lower bound of the two sided 95% confidence sample, which we believe

offers additional flexibility in obtaining the screening claim and using and including an OTC, over the counter use.

So with that, that was a lot of information, we would like to go ahead and open up this call for questions and we look forward to that. Thank you.

Coordinator: The phone lines are now open for questions. If you would like to ask a question over the phone, please press star 1 and record your name. If you'd like to withdraw your question press star 2. First question in the queue is from Shannon…

Toby Lowe: Okay. Before - sorry, before we take the first question, this is Toby Lowe, I just wanted to jump in with one additional point of clarification. Tim talked about healthcare providers ordering tests off label and since there was quite a bit of discussion about at home testing in that I just want to clarify that a healthcare provider can order a test for a different indication but not - but they cannot order a test for home use if it is not authorized for home use.

Coordinator: And with that, I will turn it back over to you to take the first caller.

Dr. Timothy Stenzel: Yes. I didn't cover that caveat. Thank you, Toby. I appreciate that.

Toby Lowe: Yes.

Coordinator: First question in the queue is from Shannon Clark. Your line is open.

Shannon Clark: Good morning. This is Shannon Clark with UserWise Consulting. We specialize in human factors testing. But I have a question about limited detection determination. So to determine a limit of detection for an antigen test kit, do you have any requirements regarding which strain of inactivated

virus is used to create contrived samples in the calculation of limit of detection?

Can we just use one US strain in order to create the contrived samples and determine the limit of detection?

Dr. Timothy Stenzel: So, you know, for molecular tests I just explained on a (Red X) call earlier this morning, some of them are going to be looking at the use of degenerate primers to make sure that they're covering the various mutations that are in circulation if they cannot engineer the assay around where they want to update their assay to maintain current levels of performance in the face of increasing numbers in locations of mutations.

It could be that in the use of degenerate primers there could be changes in LOD. So we're working through what that might look like. But for antigen tests, I think you're probably asking about for antigen tests, known variants or mutation that could affect the performance of that antigen test. Look to our mutation communication, a recent one, for how we're asking developers to start looking for potential issues with their antigen, molecular or serology tests. But I - yes, at the moment, one stream can be used for LOD determination.

Shannon Clark: Thanks so much.

Coordinator: Next question in the queue is from (Jeff Andrews). Your line is open.

(Jeff Andrews): Hi Dr. Stenzel. Thanks for taking the call. I'd like to confirm that for an EUA antigen test that - in symptomatic has a PPA above 80%, that you are saying that this new template that was released yesterday, will permit authorization for a screening claim and then - in addition to the symptomatic claim. And I

wanted to clarify whether that means that that screening claim for asymptomatics is only with serial testing or would also include one time use and whether a post market study is always required or whether that's a decision the FDA would make individually.

Dr. Timothy Stenzel: Yes. We're anticipating that the serial testing will bring performance in an - unknown performance in asymptomatic population up to an acceptable level. We will want to measure that for each device that - a test that's authorized in a post market study, to confirm the performance in the asymptomatic population reaches that 80% or more, utilizing serial testing.

So yes, a test authorized for - currently authorized for at least 80% sensitivity PPA or above, with the lower bound being 70% or greater, can seek this immediate change to a screening claim at the point of care test. And they've done all of the point of care studies and maybe already authorized, they can add a screening claim upon request by agreeing to do this serial testing program and doing the post market study.

Now the existing templates for one time use OTC and asymptomatic screening, still are in existence. So if developers want to still use that pathway and get a one time use claim that's fine as well. But for the lower sensitivity, without data in the asymptomatic population we want that serial testing as part of the authorization and we want to confirm performance in a post market study. Hopefully I addressed all of your questions. There were a few there.

(Jeff Andrews): Thank you. If I was going to ask anything else, are you going to release a template for the post market study requirements in terms of sample size, number of positives, low positive?

Dr. Timothy Stenzel: So I think that's something that you can propose in a pre-EUA when you're requesting or an EUA when you're requesting this and we can confer with you. We expect that as the current template tests for 20 positives by a comparator, high sensitivity molecular comparator method, that that is still the expectation in the post market study. So 20 positives should - asymptomatic positives should do it.

(Jeff Andrews): Thank you.

Coordinator: Next question is from (Paul Bartow). Your line is open.

(Paul Bartow): Yes. Good afternoon. How are you doing, Tim? A quick question for you. So if we are contemplating being a lab and we are running an EUA authorized serology test and let's say it's authorized on venipuncture blood, if we want to do testing using a dried blood spot does that require a full validation or is that just simply a comparison study with the existing sample method?

Dr. Timothy Stenzel: So let me just make sure I understand the question. So you have a serology test and you want to have a sample type within your healthcare network, comes to your lab of a dried blood spot. Is this for a home collection or a healthcare collection?

(Paul Bartow): I'd be interested in the answer on either one, but I was contemplating an at home collection.

Dr. Timothy Stenzel: Yes. So for at home collection that is not considered an LDT situation but a device situation. And we have posted a template already with recommendations for validating a home dried blood spot collection. So I'd refer you to that on our FDA Web site.

If you are validating that as an additional sample type for - in your lab for a kit that you're using that's authorized, you can do that within the confines of your healthcare system in healthcare environments and it doesn't require an EUA submission. However, it would no longer be an EUA, considered an EUA authorized test.

(Paul Bartow): Got it. That's helpful. Okay. Thank you.

Coordinator: Next question is from (Susan Sharp). Your line is open.

(Susan Sharp): Thank you, Toby. Thank you, Tim. Quick question - if you collect a 10 swab pool with a single swab from each person but you place it in the same transport tube for media, with the assumption that you will re-collect the specimens from each one of those 10 people for individualized testing if that pool is positive, is that initial pool testing considered screening or surveillance?

Dr. Timothy Stenzel: That is a - can you state your name again? I didn't quite catch it.

(Susan Sharp): (Susan Sharp).

Dr. Timothy Stenzel: Oh. Hey, (Susan).

(Susan Sharp): Hey.

Dr. Timothy Stenzel: Yes. I mean that is an on the edge question between surveillance and screening and I'd recommend that you come in with a question into the Template email address with that question. Typically, when I've talked to people who are doing diagnostic or screening, looking at screening, they will

collect two swabs at the time of collection and will retain the second swab in order to deconvolute that.

Typically, diagnostic or screening testing provides results directly to an individual. If something's done purely for surveillance purposes following all the FAQs and guidances that are provided by the FDA and CMS and CDC, then that sort of combined pool could be used in that kind of program. So it depends. It depends on the details; it depends on following those various FAQs and guidances on how to do screening testing or diagnostic testing and/or surveillance testing.

Do, you know, whether you do purely surveillance or not - well, if you do purely surveillance do also look at our template on how to validate this type of swab pooling because it has different considerations than pooling media. In particular, with pooling media you're more concerned about losing sensitivity (dissolution).

When you're pooling swabs the concern has to do with do you concentrate any inhibition in that swab pooling, or do you push the overall viral load in that sample of a threshold that is no longer detectable by that particular assay? So we've definitely seen - we've projected it could be seen and then we've now definitely seen that if you load up a pool maybe, you know, with swabs, with a too high a viral load that you can get a false negative on that pool and that would be unfortunate.

So I'm sorry I can't be a little bit more definitive but it does depend. I'm happy to converse through the templates email box.

(Susan Sharp): Okay. Thank you. I did send in the question to the templates email and the question again, wasn't specifically answered. So I will try one more time. Thank you.

Dr. Timothy Stenzel: We'll also try to - just send it again. We'll alert the team to forward it to Toby. Actually, you can just ask them to forward it to Toby and Tim. Okay?

(Susan Sharp): Thank you.

Toby Lowe: Yes. And I think we can also, you know, clarify and this is also in the FAQs, that, you know, it does depend on what action you're taking. If the intent is to, you know, use this to identify individuals that can or cannot take some action, you know, whether it's return to school or return to work, or whatever it is, that would generally fall under screening, not surveillance. But we're happy to discuss further for your particular situation as well.

(Susan Sharp): Thank you.

Coordinator: Next question is from (Kay Taylor). Your line is open.

(Kay Taylor): Yes. Hi Tim. I wanted to follow up on the earlier question from (Jeff Andrews). So using this template, I understand that if we already have an authorized symptomatic antigen test with performance of greater than 80%, we would submit a signed amendment to our existing EUA to request a serial screening claim.

And then we would propose in that intended use, whether that is, you know, twice a week or three times. We would propose our intended use. And then with that negotiation FDA would authorize and we would then be obligated to do the post market authorization study.

Would that study be - in asymptomatic, but would that then if let's say we have twice a week serial testing screening claim, that post market study would be done according to that so you'd want to see, you know, whatever you're trying to claim in the intended use, whether it's two or three times a week, you'd want to see that design in the post market study. Did I understand that correctly?

Dr. Timothy Stenzel: That's absolutely correct. When it comes to OTC use we're anticipating that most developers will choose to send instead of a single test, but two tests per package, using this pathway. And they would instruct the user to test on day one and day two or day one and day three, day one and day four or something like that.

And we would be looking for confirmation of whatever specific scheme you would call for, for your serial testing, is validated and shows adequate performance.

(Kay Taylor): And this would be true whether your point of care going - a point of care device or an OTC device going for this. Correct?

Dr. Timothy Stenzel: Correct.

(Kay Taylor): That wouldn't change. Okay. Thank you very much. That helps, Tim.

Dr. Timothy Stenzel: Okay.

Coordinator: Next question is from (Kodumba Venkamp). Your line is now open.

(Kodumba Venkamp): Good afternoon. Thank you for taking my call. Thanks for giving the update about - the new update about the screening and also about the two serology templates. My question is related to that serology. Again, is there any screening test for serology that you are contemplating? What is the position of FDA on serology testing now that more than 70 million people got vaccination so infection is with vaccination?

So is there any guidance for serology and in fact, you know, there are many serology tests that have more than 95% sensitivity specificity but they're all low priority and that is not even being reviewed. We are adding more and more new screening tests. So if you can (throw) some light on that I'll appreciation it. Thank you.

Dr. Timothy Stenzel: So when you're talking about a serology test in screening its use could be considered for screening for a donor selection for a convalescent plasma donation. It could also be screening for people for measurements say of an immune response that may imply with data supporting it. You know, and some sort of immunity or neutralizing antibody.

And, you know, it's made some developers talk to us about, you know, can they use their serology test to inform whether somebody has responded adequately in their adaptive immune response to a vaccine? I want to alert this audience that we have started hearing reports that some are using - some clinicians are ordering a serology test after vaccination.

And some of those test results are coming back negative unexpectedly and there is some concern. And when those investigations have been done it turns out that that vaccine generates an antibody to a spike protein but the serology test is directed towards the endpoint. So that serology test obviously is not

going to be the ideal candidate to - for a clinician to order off label a test to take a look at response to vaccine.

We remain open as has been expressed before multiple times, to additional claims around serology tests. I think what I would say is we want to make sure and expand upon what I've just said about selecting the appropriate serology test to look for immune response from a vaccine. And so we'll be looking at various pathways to do that and make sure that that's clear to laboratories and ordering clinicians.

So yes, again we're open to these sorts of things. We make decisions based on good science and data for a particular serology test and a particular indication. And as I've just said, it may come down to the specific vaccine as well, whether a serology test functions for that specific vaccine.

We also have stated that very high throughput tests of all categories, are a priority. But low throughput, non-point of care, non-home tests are currently and not - we don't envision making those a priority. We are looking to expand as fast as possible on the available testing for COVID-19, you know, from where it is now several fold higher per day.

And that's - and also expanding access, so that's going to be achieved with the higher throughput central lab test as well as access to point of care testing and home testing and home collection. So those categories still remain a high priority.

(Kodumba Venkamp): In fact, you know, conventional immunology by example, really can tell us about the recent infection. So just now, how you are mentioning about the serial testing, we have done the antibody two different times find very clearly can indicate recent infection. Another thing is when you say the

high throughput testing, high throughput testing where the serology is using high throughput and what is the definition of high throughput where you need a serology high throughput testing?

Dr. Timothy Stenzel: So that is potentially a fluid target as the pandemic goes on. So if you have questions about whether your specific assay and assay format works well, meet our current throughput expectations for review, just reach out either in a pre-EUA or to the templates email address. For those tests that are already submitted, we do that review and prioritize accordingly.

(Kodumba Venkamp): Thank you.

Coordinator: Next question is from (Richard Montagna). Your line is now open.

(Richard Montagna): Yes. This is (Richard Montagna) from (Rionics). I've called in a few times and thank you very much for the responses because they've all been very, very helpful. We have a PCR based test that's authorized for use in either respiratory or saliva specimens, and we're now working to develop a saliva self-collection kit. And as you had recommended to us two weeks ago in a town hall meeting, we have submitted the pre-EUA to outline the usability studies.

My question is, we see this being used in two different settings - one would be home collection where the kit would be sent to a home user and they would collect the saliva and ship it back to the lab. And the second use would be what we're kind of calling batch collection, which kind of ties into your opening comments of screening at schools and places of employment, etc.

So my question is can - when we submit the EUA can we lump both of those uses in a single EUA? And from an intended use standpoint, kind of lump them both together? Or how would FDA see that working?

Dr. Timothy Stenzel: Yes. So I think what you're talking about - well so home use has home collection, I would look to the home collection template and that will give you some good indication for the validation studies for home collection.

(Richard Montagna): Yes.

Dr. Timothy Stenzel: I would encourage you to potentially use collection devices that have already been authorized for other assays, because most if not all of those vendors are willing to give developers - right a reference letter that allows us to use their data for your submission so you don't have to repeat a lot of the studies. At that point it would be basically making sure that that collection device works with your particular assay.

(Richard Montagna): Yes. We were actually intending to use - excuse me. We were intending to use the same collection device that we use when we had saliva authorized. So it would not be a new device coming in.

Dr. Timothy Stenzel: Okay. Okay. Well that's fine. Just look at the additional home collection. It also would apply to remote collection other than the home that would be used for shipping say overnight, versus collecting and immediately transporting within your current time scheme. I think you're also talking about pooling saliva?

(Richard Montagna): Not in this particular submission.

Dr. Timothy Stenzel: Okay. Okay.

(Richard Montagna): We do have an EUA in there right now for pooling. But we're just talking about…

Dr. Timothy Stenzel: So once you get…

(Richard Montagna): Go ahead.

Dr. Timothy Stenzel: Yes. It also depends - I mean if you want a screening claim there are the recommended validations for screening plan and you'd get an OTC. If it's - if you were to do a home prescription collection validation that would work anywhere somebody writes a prescription for that collection method and your test, whether it be at schools or at home.

(Richard Montagna): So this would be sort of a generic prescription for a mass of people?

Dr. Timothy Stenzel: It would be a generic for - if it's under prescription, a generic for whatever claims you come in with. If it's for a symptomatic individual's alone then for - if you've got the - all the stability and usability studies then once we authorize say for home prescription use that device could be used in any prescription setting other than the home as well.

(Richard Montagna): Okay. Thank you very much.

Coordinator: Next question is from (Shanna). Your line is open.

(Shanna): Hi. Thank you so much for taking my call today. I would like to ask you about the serial testing for screening purposes. My lab is (SDI) Labs. We are a CLIA lab and we are working on over the counter antigen tests that would be then reflect into a molecular test. So I just want to ask a few questions just

to get confirmation of what was discussed in the last meeting, last week's meeting.

I understand that the FDA would like to know the demographics of the person who's taking the test and if the results came up positive or negative, because I understood that it is not a requirement for the person who's taking the test to register their results.

Dr. Timothy Stenzel: I want to clarify what your question is. You're talking about reporting requirements?

(Shanna): Yes. Yes. Reporting requirements for over the counter, you know, antigen tests.

Dr. Timothy Stenzel: Yes. So if it's an over the counter test and it's performed at home, outside of the laboratory, there is no legal, federal legal requirement to report the results of that test. We are encouraging developers to provide an option for OTC users to report their results if they so choose. They cannot be compelled.

We, in our authorization, do recommend that patients report their results to their healthcare provider so that their healthcare provider is aware of that and potentially can help them out. So there is no requirement for, pre-authorization requirement for a test to have a reporting feature for any type of test, let alone a home test. So I hope that clarifies that.

(Shanna): Yes. That does. I have a follow-on question if you don't mind.

Dr. Timothy Stenzel: Okay.

(Shanna): So we would like - okay, so with our over the counter test, antigen test, there would be an algorithm that would, you know, determine whether this individual is highly likely to have COVID-19 or not and then we would have them (reflected) to a molecular test and send it back to us. What are your thoughts on it? How - what is the priority of your organization, of FDA for such a test on the market?

Dr. Timothy Stenzel: So home tests are a priority. So you're talking about a piece of software that would be developed that would determine who gets tested in which form or way. And we are currently considering that a software as a medical device. And so the software would be reviewed as well as the testing program. And so you should look at some of the software requirements for such determination.

And we will be looking particularly at the benefit/risk of that kind. In particular, we don't necessarily mind that more people get reflected to a more sensitive test, but the risk is higher if you're eliminating people with your software, who might actually be positive for SARS. And so that is a little bit riskier calculation.

So if you want to come in with a pre-EUA for that sort of triaging software idea or whatever information you have on that, and ask us what we think we can authorize around that, we would be open to it.

(Shanna): Thank you. And so yes, but just bear in mind that we do intend to send in two tests along with, you know, for our over the counter. It won't be one test that we would have asked them to take a test again within three days if we think that they are high risk or, you know, they came up negative on the high risk. And they send us back the same samples that they have collected for molecular testing.

Dr. Timothy Stenzel: Oh okay. So yes, I think, you know, it depends. It's going to be in the details here. It's a little bit hard on this call. But in some ways it sounds like you're mitigating risk with this software and that would be a lower risk review. Okay? But I think it's - the most important way is to give you definitive details on this program to submit a pre-EUA so that we can review your proposed plan and give you specific feedback.

(Shanna): Okay. Thank you.

Coordinator: Next question is from (Nesha Lee). Your line is now open.

(Nesha Lee): Yes. Thank you for taking my call. My question is regarding the use of retrospective specimen. I know you had reiterated the requirement of having the 10% to 20% of specimens being low positives to represent natural distribution of viral loads. I'm wondering if there are any requirements on moderate or high positive sample representation if for example, having approximately 50% of the retrospective being high positive and maybe 35% being moderate. Would that be something that's acceptable?

Dr. Timothy Stenzel: So what we're aiming is to try to mimic the natural distribution of a virus CT seen over a period of time after initiation of symptoms or for asymptomatics over a period of the program. We normally see when a prospective trial, a very usual sort of spectrum of high to low positive samples. And when people use banked samples we just want to reflect that.

So there will be high positives, there will be low positives and there will be moderate positives. And that's the primary consideration. I would - if you're having a method we want to eliminate bias. So typically it's good to run your study design for using banked samples by the FDA through the pre-EUA

submission, to make sure that depending on how you're doing it that you're not introducing bias that would prevent us from making a positive regulatory decision.

So typically, when we use banked samples we want to use consecutive samples collected from one date to another rather than sort of selecting individuals in between others. So that we see sort of that more normal distribution. I would also caution and I've seen this happen, where a particular method of collection and types of banked samples that might be used, that it overemphasizes the low positives and it does have a tendency to show a poorer performance for the test and we're not wanting to do that.

So, you know, be sure that the banked set of samples you're going to, reflects the normal distribution. And then if you randomly set - select those from one point in time, calendar day to another calendar day, all the intervening samples, positive and negatives, you're going to eliminate bias and you're going to help ensure that you don't have an overabundance of the low positives.

And if you want a more detailed response than that I suggest submitting a pre-EUA to our team.

(Nesha Lee): Okay. Thank you very much. And just a quick question, I know you have mentioned that there's an update for the serology template which includes variant testing. Will there be an update on the antigen template soon? And if our EUA studies are completed before that new variant testing requirement comes out, should we submit or should we obtain the variant testing data before submitting?

Dr. Timothy Stenzel: So, you know, go ahead and submit now. We tend to - if someone submits something before we make a template update we want to, as much as possible, adhere to a prior recommendation as the fair thing to do. Unless there's clearly a high safety concern and we need to change that. But I don't see that happening right now. So we are revving the other templates that are main templates - serology, molecular and home. So be on the lookout for that. But I can't predict when they'll be posted.

(Nesha Lee): Okay. Thank you very much.

Toby Lowe: And you could also take a look at the, excuse me, the viral mutation guidance that we put out which does signal the direction that we're heading. And then, you know, as Tim said, we'll be updating the templates to reflect some of that as well. You know, and if there is something that changes it may be a post authorization consideration as well.

(Nesha Lee): Okay. Thank you very much. I appreciate it.

Coordinator: Next question is from (Johann). Your line is now open.

(Johann): Yes. Good evening. Can you hear me?

Dr. Timothy Stenzel: Yes, we can.

(Johann): Hello?

Toby Lowe: Yes.

(Johann): Okay. Wonderful. I just wanted to come back on serology testing for monitoring the reaction of vaccinated individuals. Maybe I have missed it in

some of the journals, but did you actually already put up such - something like a guideline on numbers that one should test for maybe expanding the intended use claim for an already EUA serological assay?

Dr. Timothy Stenzel: Yes. So can you restate that question? I want to make sure I understand. I think you're taking an already EUA authorized serology test and can you update the indications with additional submission in data?

(Johann): Yes. The question would be whether there are specific protocols already available that I could rely upon in order to plan the experiment or the sample collections from - for the cohorts of vaccinated individuals in order to…

Dr. Timothy Stenzel: It would…

(Johann): …(unintelligible) to…

Dr. Timothy Stenzel: Yes. Go ahead. Finish. Yes. What is it?

(Johann): In order to kind of - we have those are the claims that I, with this spike based assay can measure the specific (IGT) reaction after vaccination.

Dr. Timothy Stenzel: Okay. So this would be an after vaccination. So we don't have any recommended authorization suggestions, study suggestions for that. So I would urge you to come in with the best plan you can come in with of - with probably a pre-EUA is the way to go and suggest a study design that we can discuss with you.

(Johann): Okay. And that would also be the way if the test is already submitted and confirmed by you?

Dr. Timothy Stenzel: Yes. Yes. I mean that would be an additional claim for which we don't have current recommendations on how to validate the test for measuring effectiveness of vaccine.

(Johann): Yes. Okay.

Dr. Timothy Stenzel: Vaccinations.

(Johann): Okay. Good. Because it's - I mean it's clear. By choosing the correct assay with spike as an antigen of course, in the lab-based situations, we can see it that the reactivity is quite well measurable, but it's just a question of how to expand claim that we did not have.

Dr. Timothy Stenzel: Yes.

(Johann): And did not include.

Dr. Timothy Stenzel: I think there's different levels of claims. So I mean there could be one level of claim that says oh, this antigen test, you know, is able to detect antibodies raised by a certain vaccine. It's entirely different to say that those antibodies are protective against infection. So it all depends on your intended use claims about what sort of validations would be required.

(Johann): Okay. Okay. Good.

Dr. Timothy Stenzel: Okay.

(Johann): Yes. Thank you. That was all.

Dr. Timothy Stenzel: All right. Thank you.

Coordinator: And now I'd like to turn the call back over to Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions during today's town hall. Today's presentation and transcript will be made available on the CDRH Learn Web page at www.FDA.gov/Training/CDRHLearn, by Friday, March 27. If you have additional questions about today's presentation, please email CDRH-EUA-Templates@FDA.HHS.gov.

As we continue to host these virtual town halls we would appreciate your feedback. Following the conclusion of today's 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. Again, thank you for participating. This concludes today's virtual town hall.

Coordinator: This concludes today's call. Thank you for your participation. You may disconnect at this time. Speakers please standby.

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