

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

**Moderator: Irene Aihie
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Coordinator: Good afternoon and thank you all for standing by.

For the duration of today's conference, all participants' lines are on a listen-only mode until the question-and-answer session. At that time if you would like to ask a question, press star, 1.

Today's call is being recorded. If you have any objections, you may disconnect at this time.

It is my pleasure to introduce Miss (Irene Aihie). Thank you, ma'am. 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 seventh in a series of virtual town hall meetings to help answer technical questions about the development of validation of tests for SARS-CoV2 during the public health emergency.

Today Timothy Stenzel, Director of the Office In Vitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality and (Sara Brenner), Associate Director for Medical Affairs, both in CDRH, will provide a brief update. Following opening remarks, we will open the lines for your questions related to today's discussions.

Now I give you Timothy.

Timothy Stenzel: Hello and thank you for joining us again today and I also want to thank all of you who are engaged in this emergency to help people. That's my focus every day is how can I advance from my position, how we can help patients and help us get back to normal as soon as possible as a nation and to help the rest of the world as we can at the same time.

As has been said many times throughout this pandemic, every step the FDA has taken, an approach that carefully balances risks and benefits, we are striving to anticipate and meet the constantly evolving public health needs of this unprecedented public emergency.

That's why earlier this week we did update our policy and guidance on COVID-19 antibody tests. Most notably we are changing the policy as it applies to commercial manufacturers, those kit developers out there right now.

Under this new policy, the FDA has outlined expectations for antibody test developers, including of course kit manufacturers, which will - who will submit emergency use authorization requests with their validation within ten days from the date they either notify the FDA of their validation testing or from the date of the publication of the policy, which was Monday this week, whichever is later.

Our efforts to date have supported the availability of antibody tests which are an important tool in our fight against coronavirus. High-quality tests are serological or antibody tests, rather, or serological tests can help us understand a person's or population's exposure to the virus and their response to it.

When we issued our original serological test policy in mid-March, it was critical that the FDA provide regulatory flexibility for serological test developers, given the nature of the public health emergency and also the understanding that tests were not to be used for COVID-19 diagnosis, a fact that remains true until today and through today.

We have authorized quite a few serological tests now through the EUA process and so really at this time it was appropriate to take another look at that policy and to make a change. And that change is of course, as mentioned, that we expect all kit manufacturers to come in within the ten-day period, and our performance expectations are also laid out in this updated policy guidance.

So there are two templates attached to the guidance at the end, one for kit manufacturers and the other for high-complexity labs. The policy is still voluntary for high-complexity labs so they're welcome to submit EUAs and the performance expectations for those validations are in that template.

So at a high level, the performance expectation for serological tests going forward is that the overall sensitivity, whether it's not broken up isotype or a single is a single isotype of combined is 90%, 90 percent. And the combined or overall specificity should be at least 95%.

If isotypes broken out, the expectation is that the specificity should be at least 95% per each isotype and then sensitivity, the expectation is that IgG, if reported out separately, would have a sensitivity of at least 90% and then if

IgM is reported out separately, that the sensitivity for IgM remains at - should be at 70%.

So, again, these tests are not to be used for the diagnoses of COVID-19. They are expected to inform about the presence or absence of antibodies. As has been mentioned previously, if it's important to know whether an antibody test really is specific that a second confirmatory serological test utilizing a different antigen should be considered as well.

The combined dual-positive results requirement, if you follow that path, if you choose to follow that path, greatly - has the potential to greatly increase the specificity. In the end, it does increase substantially, in theory, the positive predictive value of a positive result that is the likelihood that a positive result is a true positive.

There's still the chance that it - that even after two serological tests you could still have a combined false positive result, given that few, if any, tests are 100% specific. However, this confirmation test, if used, should greatly increase the predictive power of serological tests, if that's important for a given patient or for a population study.

Now it's also been known since last week that there's been a collaboration on performance testing at NCI. This has been a great federal collaborative effort involving of course also NIH, BARDA, CDC and the FDA. Testing has begun and we will report results from that testing when we make regulatory decisions if testing has been done in that program.

When we make regulatory decisions going forward around serological tests we will of course as always take in the totality of the evidence, presented both by the test developer, if testing is done at NCI, those results, and other

information that we may glean about the performance of a given test. That may be publications, reports from other government agencies, et cetera.

So when we make that regulatory determination whether a test is authorized or not, any testing at NCI will be made public. In fact, earlier this week we did authorize the EUROIMMUN IgG test. That is listed on our EUA authorization page and we also created a new page which lists the performance by test.

We are doing our best with that page to very clearly display the performance of each test with regard to sensitivity, specificity, as well as some other factors that may be appropriate. We also give the 95% confidence intervals for those tests and we feel that awareness of the 95% confidence intervals is important because the sample sized used, though sometimes very significant, still have a statistical margin for error, should we say.

And so in evaluating a test using the 95% confidence interval to understand what the potential performance range might be for a given test in a given number of samples tested. On this page, we also list the positive predictive value and the negative predictive value at a prevalence of 5%. Of course your population that you do testing with these tests may be different than 5%.

As a result, on our website we - on the EUA authorized serological test performance website in the FDA we now list a calculator that you may use. This calculator allows you to input test performance, either a single test prevalence for your population and if you're going to use a two-test strategy, you can put in the performance, the sensitivity specificity - calculated sensitivity specificity for the assay, along with the prevalence and it will give you the combined performance as predicted.

This is not actually because we have not validated the actual performance with

two tests but it is a potentially useful tool to try to get an estimated performance of either a single test or two independent tests.

That sort of is the end of my opening remarks as regards to the updates for serological testing. I did want to briefly mention that we added other updates to our FAQ page. We have updated the page to address of molecular tests at least, the testing or screening of a symptomatic individual. So that should have been posted already. And so the question has been frequent and so we wanted to post the answer that we've come up with.

At this time most EUA-authorized SARS-CoV2 molecular diagnostics are authorized for use in individual suspected of COVID-19 by their health care providers. Testing of asymptomatic individuals who are suspected of COVID-19 are is at the discretion of the health care provider ordering the test.

All tests should be appropriately validated for the intended use population. If you would like to develop and offer a test with an intended use, including board screening of any asymptomatic individuals, please reach out to our templates email address to discuss the validation necessary to support an EUA for such an indication or claim for performance of your test in an asymptomatic population.

So hopefully that information is helpful to the community and to potential developers. And one other update is that we did provide serological tests development templates for both IVD kit manufacturers as well as laboratories who develop a test and that is downloadable in editable form to make it easy to use. So please check out our website.

And with that, I don't believe that (Sara) had any comments to start off so we can open it up for questions. Thank you.

Coordinator: Thank you. If you would like to ask a question, please make sure your phone is unmuted, press star, 1 and record your first and last name clearly when prompted so I may introduce you. Again, that is star, 1 if you would like to ask a question.

Our first question is from (Shannon Clark). Your line is open.

(Shannon Clark): Hi. This is (Shannon Clark). Can you hear me?

Timothy Stenzel: I can.

(Shannon Clark): Oh good. This is (Shannon Clark) with (User Wise) Consulting. We have expertise in home routine and factor assessing for medical diagnostic. We did send you an open-sourced simulated use protocol based on a protocol we co-developed with the FDA-CDRH human factors team.

So the question I'm about to ask is a do you agree or disagree question. Typically when we run single (unintelligible) human factor testing we don't permit (unintelligible). They're to follow instructions for use and we may or may not be able to train them if they would not typically receive training and also these studies are not typically based on questionnaires.

The CDRH human factors guidance I quote, it says, "Observational and knowledge task data should be supplemented with subjective data collected through interviews with the participants after the use are completed so there's no intent to assess ease of use per se and that's not what we typically do as part of these studies but the guidance offered by the FDA lately has kind of focused around ease of use. And I think that's led to confusion, maybe confusing companies into thinking that this is sort of a questionnaire-based

activity.

So that was sort of a comment and I didn't know whether maybe you might want to connect with the CDHR team and factors team to align a little bit better. And then also simulated use is typically sufficient for most human factors testing so I guess I'll end my question and say do you agree or disagree with all that.

Timothy Stenzel: So great questions. You know, in an attempt to adequately address this emergency and to make sure that as we move into home collection or home testing that we ensure the accuracy of those tests, we are taking steps to try to assure this through the accumulation of data to justify that these technologies can be accurately used.

So I think the - I will double-check with our team, although I'm sure they're familiar with the human factors group at the FDA and make sure that we are aligned, to the extent we can, under this emergency and I think that that's a good thing for me to check on.

We are working on a template for home collection. We hope to make that available in the not-too-distant future. We will then turn our attention - and we also are working on an antigen, a direct antigen template, and then after those we will begin working on the likelihood that we will be seeing home tests applications as well. So we'll turn our attention to developing a template for that to help developers as well.

(Shannon Clark): I'm wondering though about your position about simulated used where there isn't - so, for example, capillary blood, the idea of having a user actually administer a finger stick, if you're having health care providers do it, at least I think many in the human factors community believe that a simulated use

assessment would be sufficient and then you could separate out sort of real blood in a separate study, like a flex study. Does that make sense?

Timothy Stenzel: We're open to taking a look at that. At this moment when we require so little relative to our normal procedure of data, we do want to make sure that these things are appropriate. We have seen a lay and patient and consumer test results from the methods that we're using now and we know that not all users may follow a given set of directions very well.

And so our attempts really twofold. One is to ensure the safety of the process and the second is the accuracy of the process. And at the moment, while we remain open to these other suggestions, we feel it's important to assess this performance right now in this emergency with actual patients or simulated patients.

(Shannon Clark): Yes. In our study, we typically expect about 30% to actually pick up and follow the instructions if not prompted to do so.

Timothy Stenzel: Yes. Yes, it's a challenging situation but thanks for your questions. We'll move on here. Thank you.

Coordinator: And our next question is from (Tim Salter). Your line is open.

(Tim Salter): Good afternoon. In the last meeting there was a question posed in regard to non-laboratorians performing point-of-care testing outside of the CLIA complex lab. Does the FDA object to the use of IVDD serology antibody rapid tests outside of a laboratory by health care professionals?

Timothy Stenzel: So we make a - first of all those serological kit developers that have notified us if they have not received EUA authorizations, they are designated to be

high complexity. That was an important element of the prior policy to ensure that, to some degree, these tests that were not previously reviewed were performed in an excellent manner and also that the laboratory did perform their verification and their validation of those tests to ensure accuracy prior to putting them into service.

So when we review a potential point of care and near-patient test, we evaluate whether or not that test can be performed outside of a moderately or high-complexity lab and we so designate under this emergency in a way that allows for flexibility in where the tests can be performed. It is not, unless there's specific authorization for home use, it's not authorized for home use. That needs to be made clear.

However, we do not as the FDA say exactly where a test should be performed. Rather there are other agency requirements that - and I would refer you to CMS and their recent information about this - but it's my understanding, and confirm with CMS, that if you're outside of a moderately or high-complexity lab, you do require a CLIA certificate to perform that, a CLIA-waiver certificate to perform that testing or the equivalent.

(Tim Salter): And I understand that from the - from a perspective of, you know, an instrument-based test but in the case of a rapid test where it's intended to be used, you know, by health care practitioners at the point of care, am I understanding correctly that places like doctor's offices or other types of urgent care clinics that wouldn't necessarily have some sort of CLIA license would not be able to use those types of point-of-care tests?

Timothy Stenzel: There are actually, to my understanding, quite a few CLIA-waived sites in the US and I believe, and I would confirm with CMS, that they're very open for business and will work a provider to generate new certificates as may be

needed.

And I guess, you know, it's not really a question that I can answer because that's not in our regulatory purview but it's in CMS's. We assess whether or not a test can be accurately performed outside of a high-complexity or moderately complex lab and then make the assessment about whether it can be a waived type test or a deemed waive test.

(Tim Salter): Okay. So just to clarify that, at this point there's no objection from the FDA for the use of these devices outside of the CLIA sphere?

Timothy Stenzel: It's our understanding that these tests should, even if they're point of care, near-patient, they should be performed in - under a CLIA certificate of waiver situation. So that's about all I can say.

(Tim Salter): Thank you very much.

Coordinator: And our next question is from (Grant Mitler). Your line is open.

(Grant Mitler): Hi, Dr. Stenzel. It's hard to know which question to ask but let me - the question - let's talk about the guidance that was issued May 4 with the templates and could you clarify now the relationship of the umbrella pathway to this guidance and specifically could you clarify the - if a manufacturer wants to get the voluntary testing program going by sending 125 test kits to the NCI, can that process be sort of jumpstarted?

Can those kits be sent in while they're also getting either the pre-EUA or EUA in? And as part of the question, is there such - is there still such a thing as a pre-EUA?

Timothy Stenzel: Yes. A pre-EUA is basically an opportunity to come in and ask questions. It might be, you know, is this an adequate way to validate a test or, you know, for a CLIA-waived test, something like that. Now that we have - the pre-EUA pathway though was a little bit more important when the templates weren't yet finalized and made available.

Now that they're finalized and made available, we hope that there's enough information there for all the common variety uses. There will still be some special cases. We - for example, saliva could actually be a sample type for not just molecular but serological tests and even direct antigen tests.

So we still view that sample type as something that we want to carefully look at and would engage. But it's our hope that going forward if there's a possibility, say, that saliva might be used, that we'll provide some recommendations in the template for saliva.

So I would encourage folks to utilize the information in the templates as much as possible. Our team is very, very busy so we're there to help out as needed but hopefully by providing this additional information in the form of templates, the need for a new requirement or, you know, the importance of, you know, going and discussing your device and your study with the FDA may be minimized. So this kind of makes it easier for all of us.

As far as NCI, yes. You can reach out to the templates email address (CDRH-EUA-Templates@fda.hhs.gov) and request the opportunity to send your test to the NCI and we would probably do an assessment now because there's been quite a strong interest and, you know, we would assess whether or not NCI testing is warranted or not, depending on what validation you may have already performed.

And so we may be a little bit more strategic in the use of NCI resources and how we go forward with that. So please do contact us if you're interested. Now you also asked about what the difference is between the umbrella and this new guidance on Monday this week.

So the umbrella was designed for companies that wanted to basically utilize the NCI testing for supporting their EUA authorization. Now since - at NCI we're at the moment limiting testing to serum and plasma, the sample types that are allowed under that umbrella are limited to serum and plasma, and there are many developers who wish to have more than that and so they may want whole blood, they may want finger stick.

The other thing we couldn't assess under that regulatory pathway, the umbrella pathway was saying near-patient testing, lay-user testing and certainly not home testing or home collection. So the umbrella is really kind of a streamlined pathway for those developers that have a serum and plasma tests and the testing - and the testing of the device could be essentially composing at NCI without any additional testing for those narrow uses. So hopefully that's a good explanation.

(Grant Mitler): Thank you.

Timothy Stenzel: You're welcome.

Coordinator: And our next question is from (Sue Warner). Your line is open.

(Sue Warner): Yes. Good afternoon. Actually my question sideways directly from the last question so it was actually very good timing. And what I'm interested in understanding is for manufacturers that have submitted tests to the evaluation program that you were just speaking of and understanding the lead time

considerations with the volume of testing that NCI is ramping up to do, can you comment on how manufacturers should manage any results from that testing with the need to submit an EUA by May 18?

Timothy Stenzel: Yeah, so the requirement to submit an EUA exists whether or not you've utilized the NCI testing pathway. Simply notifying us and saying that it was never really an option, well I'm going to submit it to the NCI and that's going to be my validation, so that's not a notified pathway. If you are intent on using just the NCI data, then we would want to work with you or any such developers to just be along the testing. Again an email to the template's address if you haven't been assigned a primary reviewer, we can give you an update on the status.

But we do intend to, where for those folks that either submit tests to the NCI or we have a request that they submit their test to the NCI, we will use that information in our decision making. Also I'd say that the guidance on Monday didn't change the fact that test developers can still notify us as long as they file within 10 days a EUA and they can market and stay on the market while we do our review.

(Sue Warner): Okay, thank you.

Talya Simpson: And our next question is from (Daniel Simpson) your line is open.

(Daniel Simpson): Yeah, hi Doctor Stenzel.

Timothy Stenzel: Tim, please.

(Daniel Simpson): Yeah, my question is regarding if a developer is considering doing the umbrella pathway, if the NIH stamp holder being used if there was some

characterization data that could be provided to the developer so they understood the level of characterization of the samples.

Timothy Stenzel: Yeah. You can address that question to get specific answers at our templates email address. But the inter-agency group is really focused on pulling together high quality samples for which we have well documented understanding of those samples. With the positive samples, we typically use two separate reference methods to establish the presence or absence of IgM or IgG. And then the negative samples are typically pre-COVID-19 and to the extent that we can utilize specific, known histories of exposure to other pathogens that we incorporate that as needed.

Also as we move from say one bench of samples to another, we are trying to harmonize those efforts, but since we so carefully characterized these samples, and they are known to be either IgM or IgG positive, and it requires multiple tests in most cases to verify that a sample is negative or positive, that this really represents a situation that maybe a little bit easier for some developers because these samples are so well characterized. So we don't that this puts any developers at a disadvantage, we're open to hearing if anybody thinks that would. And so therefore I think we can expect very high performance of counts that go through that pathway.

(Daniel Simpson): No that sounds great, thank you very much.

Talya Simpson: And your next question is from (Jason Obrahim), your line is open.

(Jason Obrahim): Thank you. I was wondering, for manufacturers submitting tests for evaluation to the NCI, I believe for the LDTs it was required that 125 tests be sent. It's at a 96 test kit is being sent, such as the You're Immune test that received approval. How many of those kits would be required? And also do you

recommend that for the manufacturer going through the NCI validation, should they still submit an EUA application at the same time or should they wait for the umbrella pathway?

Timothy Stenzel: If they have their own data to support their validation, I would recommend getting the EUA application going. And you can note in that application that you've requested to send tests to the NCI for inclusion in the evaluation of your test. And then as far as the number goes, that's a great question to send to our templates address. Those that aren't lateral flow devices, we do want to make an assessment to make sure that we have the capability of performing the testing for those particular devices.

You know, do we have the correct instrumentation et cetera? And as far as the number of tests for that situation, I'm unfortunately not the one to ask, but you're correct, some of them are not lateral flow, and the actual requirements for us would depend on the technology. Yeah, that's a great question for the templates email address (CDRH-EUA-Templates@fda.hhs.gov). So thank you.

(Jason Obrahim): Thank you.

Tayla Simpson: Our next question is from (Wes Wilson), your line is open.

(Wes Wilson): Hello, hi. My question has to do with the authorized settings for EUA tests and non-EUA tests. Now you've done a great job in defining, under EUA, the three categories for authorized settings H, M and W for a test that has been EUA certified. My question is with regards to the serology lateral flow tests that do not have an EUA. Under Section D in your new guidance, it indicates that unless and until an EUA is issued, the authorized additional testing environments is limited to highly complex laboratories. If this is true, why

isn't this more clear? So that we understand that only highly complex laboratories can actually run this test?

Timothy Stenzel: So we've attempted to be clear in our FAQ page as it regards to the list of notified users and if they have not yet notified developers, rather in Section D. And we attempted to make this very clear in terms of what hasn't been authorized, the complexity categorization, and eventually hopefully point of care waived testing. We do show the designation, even for those tests that have not been authorized so in order to classify a test as moderately complex or waived in current in what you see, it is required that we actually make an authorization decision before we can do something to be suitable for moderately complex or waived.

And so that's unfortunately the limitation of the notification pathway, that even though a test may be designed for a moderately complex lab, and/or a waived environment, we cannot deem it as such until we have reviewed it and made an authorization decision.

(Wes Wilson): So that means that they could only be used in highly complex laboratories until the EUA has been issued and then further designated. Is that correct?

Timothy Stenzel: That is correct. Although there are potentially highly complexity labs that have an opportunity to do point of care type tests.

(Wes Wilson): But that point of care test...

Timothy Stenzel: It doesn't preclude them for using it in a more flexible manner as long as they carry a highly complex certificate.

(Wes Wilson): Right, exactly, that's my understanding. So we are clear on that. We

understand that the highly complex facilities will have point of care testing, but it's still under the aegis and guidance and certification of that highly complex laboratory, right?

Timothy Stenzel: Correct.

(Wes Wilson): Correct, okay. Thank you. Thank you for the clarification.

Timothy Stenzel: You're welcome.

Tayla Simpson: And your next question is from (Chris Kepi), your line is open.

(Chris Kepi): Hi there, thank you to everyone on the call and at the agency, you guys have helped a lot of with this process. My question relates to access to testing, especially as businesses are opening up. Some employers' labs and other interviews we've been working with have indicated that the RX only requirement is a real impediment and they're also struggling with the intended use statements that are limited to individuals suspected with COVID-19 by their healthcare provider.

So for RX only, we in state law already have controls on test ordering, like who's an authorized person, and it's resolved under state law and many states don't require a healthcare provider to order tests already. While others are still waiting requirement for the space. But the RX only requirement's restricting access that works against some state efforts and the clear state law framework governing test orders. So I was wondering is FDA considering deferring to states on this issue of access instead of maintaining the RX only requirement, or does FDA have tenets or guidance regarding authorization of testing for non-prescription use?

And on the intended use front, it seems like many tests are indicated for some asymptomatic patients, but not others. Is there a difference FDA expecting to see among different types of asymptomatic patients in terms of how well the test works or what's driving the need for further validation to support general crowd testing? Thank you,

Timothy Stenzel: To answer I want to make sure that I have it. So today we have operated under the expectation that physicians or clinicians with prescribing capability would be involved in the testing to ensure that the results are accurately relayed back to the patient and the healthcare team that is making decisions.

We are open to other models and if you have a way of wanting to do that come and chat with us. I have made a note about what we can do potentially proactively with this. I know that - and I don't want to speak out of turn - that this question has come up, I just don't know if some federal entity has made any pronouncements about that, it wouldn't have come from the office that I direct. And I'm not sure where it would come from. It may be - I'm not even going to speculate, but I will take that back and hopefully provide a way to make that more clear.

We commonly use the Frequently Asked Questions page, but I don't know if you caught my statement at the beginning about asymptomatic patient testings, we now have a Frequently Asked Question about this. It really has to do with, from an FDA perspective, about whether or not evidence is provided that would allow use, or claim use, in asymptomatic populations.

I would say I've seen various reports that maybe 20% of SARS coronavirus 2 patients are asymptomatic or maybe presymptomatic and then, of course, there's maybe time periods after symptoms has resolved if they've had SARS coronavirus 2 at which point, for some period of time, they may still be

shedding virus. Whether that virus has the ability to infect others or not, may not be known at the present time.

So we have typically said that these diagnostic tests, which are not serology tests but rather molecular tests and potentially feature rapid antigen tests that these are intended for populations that are suspected of having COVID-19. Primarily because we have a better understanding of those populations.

As our knowledge grows about asymptomatic patients, and what methods may be able to be used to detect whether somebody is an asymptomatic carrier or shatter, and what sample type is best, what swab type might be best, maybe there are multiple sites, maybe there are multiple swab types that would be useful.

But for the time being and how evidence is presented in some way to the FDA, we are very open to claims around asymptomatic testing. But for now, our statement is on our website now that testing of asymptomatic individuals who are suspected of COVID-19 is at the discretion of the health care provider.

And so that can be somebody, you know, it's up to the healthcare prescriber and so we have offered from at least in FDA perspective, maximal flexibility for use of that. And again, we are very willing to authorize a test for use in asymptomatic individuals. We just, we would like to see the data that supports that, you know, what the performance in such a population would be.

For example, what percentage of asymptomatic carriers would be - would test positive. Is there any risk of false positives? So those are not necessarily easy studies to carry out. And designing them to assess whether or not somebody is an asymptomatic carrier, you know, would require some discussion with our

team.

(Chris Kepi): I guess the point of confusion and thank you, is that it seems that many of these tests are already indicated for some asymptomatic individuals and that individuals suspected of COVID-19 may describe asymptomatic individuals?

Timothy Stenzel: Yes. So what we haven't done to my knowledge is to authorize a test specifically for an asymptomatic population. But we on purpose left this a little bit open. Not yet to my knowledge allowed claims for performance in an asymptomatic population, but that we would allow this intended use for this population suspected of having COVID-19 so that it would be flexibility in the use of that test as deemed appropriate by the healthcare provider who orders the test.

(Chris Kepi): Okay, thank you.

Coordinator: And our next question is from (Sean Higgins). Your line is open.

(Sean Higgins): Yes, this is an easy technical question. I was wondering if you consolidated the for the molecular side, (unintelligible) type sequences that are in the tests and similarly, the serology side, the information about the protein components that are included in the test?

Timothy Stenzel: I was on mute, sorry. We were wanting to make sure that the deemed targets in molecular tests and now as we move forward, the antigens used for the serology tests are evident. Actual protein sequences of an antigen are the actual primers and probes used by a particular manufacturer or developer may be considered proprietary.

And so while the agency may know they are restricted in what they can

provide, however the test developers want to provide that to the community, the FDA would not be opposed to that. But at a minimum, we want to make sure that people understand what are the gene targets for molecular (unintelligible) and watch protein what viral protein is used as the antigen in a serology test.

And I think when we come to direct antigen test, what is the target of that test, what's the viral target, the protein target of the test that people can assess and study and do research and do comparative studies to understand relative performance, targeting different aspects of the virus.

(Sean Higgins): Thank you.

Coordinator: And our next question is from (Julie Leslie). Your line is open.

(Julie Leslie): Hi. I was trying to better understand the difference serology tests that already have a EUA and I saw there was a serology antibody test. Is that – would tests like that be serology total antibody? Is there a distinction or is that just a mistake (unintelligible) IgG and IgM?

Timothy Stenzel: Yes. So there's different flavors. So some test, let's say we are going to look at IgG and were going to look at IgM, there is other claims such as (PAN) antibody. We expect a test that has been developed for (PAN) anti-body will be able to detect all of the isotypes.

And then there are others that may only partially cover some of the isotypes, so they cannot claim (PAN) antibody tests. And so that's Nuance language is good pickup and we seek to have truth in advertising as it comes to a test name and a test target. Hopefully that's helpful.

(Julie Leslie): Yes, thank you for clarifying.

Coordinator: And our next question is from (William Shore). Your line is open.

(William Shore): Thank you. I appreciate you taking my question. I know that my question is concerning the 3D print swabs. I know that the results of the IRB on 3D printed swabs was provided to the FDA and I just wanted to know if there is any progress on that.

Timothy Stenzel: The IRB? I'm not sure that I understand.

(William Shore): The Institutional Review Board.

Timothy Stenzel: Yes, this may be in regards to a specific situation that the agency is reviewing. So I would just direct the question back to our COVIDManufacturing@fda.hhs.gov email address for specific feedback on anything that you may have submitted to the FDA. We are very interested in new technologies to address shortages are potential shortages. And the 3D swabs are part of that.

But if there is a specific swab, specific developer of a swab or specific question about such swabs, I'm probably not going to be able to answer it on the call today. But our team can hopefully answer that question for you in short order. You have any general questions about 3D swabs?

(William Shore): No, I was just concerned about the progress on it because I know that information was provided to the FDA and I was just curious about the review.

Timothy Stenzel: Okay. Yes, if you send – you can send an email to the COVIDManufacturing@fda.hhs.gov and they should get back to you in short

order. We've done a really good job of managing that email address, even though we've had tens of thousands of emails.

(Sara Brenner): We have. Thanks (Tim). And to the gentleman who is asking the question, this is (Sara Brenner). I know I've talked about 3D swabs on these calls in previous weeks, so please cc me on that inquiry (Sara.Brenner@fda.hhs.gov) and I will be sure to track down the specific case that you are asking about. We are looking forward to, as I said now for many weeks, providing more information on technical considerations for the community and our hope is to do that by next week.

(William Shore): Okay, thank you.

Timothy Stenzel: Thanks (Sara).

(Sara Brenner): Yes. And thanks everyone for your patience as we are working through the process.

Timothy Stenzel: Okay, do we have time for another question if there is one?

Coordinator: And our next question is from (Deborah Sigara). Your line is open.

(Deborah Sigara): Oh hi, thank you. I'm happy. It's like winning the lottery. I am (Deborah Sigara). I'm from Puerto Rico. It goes along with other questions that have been made this morning in terms of the use of molecular testing for the general population.

In Puerto Rico, we have been 50 plus days in mandatory lockdown, and this week it was (unintelligible) for some industries to go back to work. And they are looking for alternatives of what to do with their employees before they go

back to work. We are working in a group of labs. We meet three times a week and we have capacity of at least 1400 PCR testing a day.

But, I comment to them because I have been in these meetings every Wednesday what was said, but they argued that how can that not be the – the molecular test not be used for the general population when we use it and tracing when somebody is in contact with somebody else. Just your thoughts on that and see how we can better decide what to do.

Timothy Stenzel: Yes. No, that's a great question and it's a challenging situation. And although we the manufacturers have really done a great job on the molecular test, at least make the PCR readings in high abundance, a lot of high throughput manufacturers have come on to the market with UA authorizations.

But even so, the need for testing and the desire for the molecular testing has a tendency to potentially outstrip the lab capacity to, you know, return molecular results in a timely matter for if you really want to expand testing into more populations.

So that is definitely a challenge. It's definitely one that we've been thinking about and others in the government have been thinking about how to handle. Unfortunately, CMS has provided some flexibility here. The FDA has provided some flexibility as well in that we've on our FAQ page for alternative ways to do molecular testing, we are allowing an expanding number of essay PCR instruments to be used, properly validated some sort of bridging city by the lab.

And CMS has - to my understanding - given the ability to expand a (CLIA) lab to be able to use other instruments that may be on campus. So I will just refer you to the CMS memo. That said, we know that expanded testing is

really a requirement. And we are very encouraged that there are a number of developers that are developing a rapid antigen test.

Now, traditionally have not been as sensitive as molecular tests, that's a known challenge. We have been reaching and discussing tests with stakeholder communities and professional organizations. And although we know that the performance may be less sensitive, say, then a molecular test, there may still be value if users understand the performance of these tests and the proper use of these tests and the proper interpretation and use of results.

So for example, some of these rapid tests may be very specific so if you get a positive result in a short amount of time, you can probably act on it. If you get a negative result, you will want to understand what is the sensitivity of the test, what is the potential for a false negative, and use other information that's available to healthcare workers to assess what is the proper follow-up for the patient.

Perhaps it's a reflex to a molecular test in the appropriate situations. The advantage of the rapid antigen tests is that they can be produced in quantities of millions. And can it be point of care and so and obviously high yield a rapid result.

So as with everything else in this emergency, we try to walk a fine line of balancing risks and benefits and understanding the performance of various technologies, trying to address concerns with the certain issues and but the overall objective is trying to make high-quality, accurate testing available in the largest possible way. So hopefully some of those concepts and thoughts are helpful. We are working very hard with some rapid imaging and test developers in order to try to make those available in the not too distant future.

(Deborah Sigara): Thank you. Yeah, I think the most important thing will be when they go back to work to identify them as early as possible and really use those PCR tests to isolate those employees as soon as possible, but thank you. Thank you for (unintelligible).

Timothy Stenzel: You're welcome.

Coordinator: This concludes the question and answer session. I'd now like to turn the call back to Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH1 webpage at www.fda.gov/training/cdrh1 by Monday, May 11. If you have additional questions about today's presentation, please email cdrh-eua-templates@fda.hhs.gov.

As always, we appreciate your feedback. Following the conclusion of today's presentation, please complete a short 13 question survey about your FDA CDRH virtual town hall experience. The survey can be found at www.fda.gov/cdrhwebinar immediately following the conclusion of today's live discussion. Again, thank you for participating. This concludes today's discussion.

Coordinator: Thank you for participating. This concludes today's conference. You may disconnect at this time. Speakers, please standby for post-conference.

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