

**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. Today's call is being recorded. If you have any objections you may disconnect. At this time all participants are in a listen-only mode until the question and answer session of today's conference. At that time you may press Star 1 on your phone to ask a question. I would now like to turn the conference over to Irene Aihie. You may begin.

Irene Aihie: Thank you. Hello. I am Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 22nd 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 Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health and the Office of Product Evaluation and Quality and Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and Radiological Health both from CDRH will provide a brief update.

Following opening remarks we will open the line for your questions related to

today's discussion. Please remember that we will not be able to respond to questions about specific submissions that might be under review. Now I give you Toby.

Toby Lowe: Thanks Irene. Hi everyone. Thanks for joining us again. I just have a couple of updates this morning or today. It's not this morning anymore. So first we updated a couple of our FAQs regarding screening and asymptomatic testing. The intent of these updates was to make a more clear distinction between what we expect from manufacturers and laboratories that are offering the - a test for screening versus what health care providers can order.

So we indicated in our FAQs that we do expect developers of tests both commercial manufacturers and clinical laboratories to consult our templates for validation recommendations and to submit an EUA for their tests when they want to make claims regarding screening of asymptomatic individuals.

And then we also indicated in our FAQ that healthcare providers may order tests that are not specifically labeled for screening. They may order such tests for screening even if they're not labeled that way. And we include in our FAQ some considerations for healthcare providers including considering the performance of the tests that they're ordering considering the turnaround time and considering different testing approaches depending on the performance of the tests and the overall testing program that they're incorporating a test into. So please take a look at those FAQs and hopefully those will be helpful.

The next topic I wanted to touch on is we talked a little bit last week about the template for non-lab testing. And we got some questions after the town hall last week about the reference to non-lab testing and how that matched up with the CMS CLIA requirements for testing to be done in labs that are certified by CLIA. And so I wanted to make sure to provide a little bit more information

around that and what we mean by non-lab testing.

We had originally referred to this as at-home testing and we had changed our terminology to non-lab to try to be more clear that these tests may not strictly be performed in an individual's home but it looks like we may have caused more confusion. So we're working to clarify that. And we have had conversations with our CMS colleagues about this as well and we're on the same page there.

The tests that we're referring to here are tests that FDA authorizes for home use. And when we refer to home use, we're really referring to self-testing. So the self-testing can take place in an individual's home or at another setting. So that's why we had referred to it as non-lab because the - an individual who is self-testing could do so at a school or at an airport or a sporting event or any other sort of non-home and non-lab setting where there is not personnel from that facility that's involved in the testing.

So what I mean by that is you know someone at a facility like a school or a or a sporting event for example could hand an individual a test but that facility personnel could not be involved in the sample collection or the performing of the test or the interpretation of the results.

But if, you know, if there were - if we were to get to the point where we had a test that was simple enough for an individual to just, you know, perform themselves while standing outside of a building before they go in and that individual can provide the sample themselves, do whatever needs to be done to perform the testing and, you know, read and interpret the results themselves, that is what we would consider to be a self-test or an, you know, at home or non-lab test. And that's why we have put together that template for such tests that would not be performed within a CLIA laboratory.

So hopefully that provides a little bit of clarity on that topic. And then the last update that I have is on Saturday authorized the SalivaDirect test. This is a test that was authorized under an EUA issued to the Yale School of Public Health Department of Epidemiology of Microbial Diseases.

And it - the authorization specified a particular laboratory at Yale that is authorized to perform this test as well as authorized laboratories designated by the Yale School of Public Health the Department of Epidemiology of Microbial Diseases that are certified under CLIA and the requirements to perform high complexity tests.

So this is a test that we authorized for Yale and they are able to distribute their instructions for use to other laboratories that are certified under CLIA to perform high complexity tests. And those other laboratories can perform this test under this EUA as long as they acquire all the components specified in the authorized instructions for use and perform the test according to the authorized instructions for use provided by Yale. So those are the updates that I have for today. And I'll turn you over to Tim.

Timothy Stenzel: Thank you Toby and hello everyone. It's great to be on - back on the call this week. I wanted to just take just a couple of minutes to basically encourage the further development of more point of care diagnostic tests. We this week authorized the third direct antigen test and so now there are three such tests that have been EUA authorized. And we want to encourage more and there will be more.

We feel like that a rapid turnaround test that has sufficient sensitivity especially in the period that corresponds to a patient who has symptoms, acute symptoms, those are when - those days during which for the most part that virus levels are very high and, you know, are more easily detected by all tests including these

point of care tests.

And you know it's really those individuals who have monitor high viral loads that that we want to especially identify as quickly as possible. And that's where these point of care, quick turnaround time diagnostics which could also molecular point of care tests can really, really aid us in this effort. So we look forward to more submissions and more authorizations. I just wanted to push that a little bit. And with that that ends our opening remarks and we are ready to go into the question and answer phase of this call. Thank you.

Toby Lowe:

((Crosstalk))

Irene Aihie: We're ready for questions now.

Coordinator: If you would like to ask a question press Star 1 from your phone, unmute your line and speak your name clearly when prompted. Again, if you would like to ask a question press Star 1. Our first question comes from (Cynthia Flynn). Your line is now open.

(Cynthia Flynn): Hi. I wanted some more clarification on this - on the Yale SalivaDirect test. Many of us in clinical microbiology and molecular diagnostics are kind of confused because of the fact that this is an EUA that other labs could use besides the lab that developed it. So, you know, if we were to contact Yale and get approval from them to run the tests do we then have to submit any validation data to the FDA or we're just able to start running the tests?

Timothy Stenzel: Toby...

((Crosstalk))

Timothy Stenzel: ...you want to take that?

Toby Lowe: Sure, I'm happy to. So we have heard that question and it - sorry I wasn't as clear as I should have been in my introduction. A laboratory that has provided the authorized instructions for use by Yale and is designated as an authorized lab under the EUA by Yale does not need to get their own EUA.

This is sort of, you know, similar to a distributed test kit except that the components that are specified in the authorized instructions for use are generally all commercially available. So they're sort of required but not provided components of the...

((Crosstalk))

Toby Lowe: ...authorized test. So Yale would provide the authorized instruction for use and the laboratory would acquire all of those components and perform the test as authorized.

(Cynthia Flynn): All right and if you don't mind one other question. I can't see that - what the antigen test is that you - was the third authorized antigen test up on the Web site. Is it already up on the Web site or not?

Toby Lowe: I think it...

Timothy Stenzel: It is.

Toby Lowe: ...was posted...

Timothy Stenzel: Yes, the LiuraDx, yes.

Toby Lowe: ...right before this, yes.

Timothy Stenzel: Yes so LumiraDx. I was just...

(Cynthia Flynn): Lumira.

Timothy Stenzel: ...checking it now and it popped there.

Toby Lowe: Yes.

(Cynthia Flynn): Okay thank you

Coordinator: Our next question comes from (Jess Terivery). Your line is now open.

(Jess Terivery): Yes hello? Can you hear me?

Timothy Stenzel: Yes.

Toby Lowe: Yes, we can.

(Jess Terivery): Good. Yes good afternoon. I have a question on the FDA's point of view and strategy on semi-quantitative tests that which two have just been approved from Siemens and versus a full quantitation. So we have a calibration range versus a standard curve. What is the FDA's thoughts on semi quant versus quant?

Timothy Stenzel: We welcome both. We think there's value for both. There might be, you know, enhanced value if there's some sort of titer, you know, so that it goes back to more directly measuring say antibody levels. But we are fully open and

supportive of both. And we think it's a good evolution of the technology to go there and are willing to work with any and all developers.

So I don't - we don't have a preference over one over the other from the FDA perspective. You know, looking into how these various evolutions and serology tests could be used in the clinical space is evolving and important to watch and see where things are headed.

(Jess Terivery): Well thank you for that. Then just to follow-up on the EUA strategy then would it be simpler to submit first a semi-quant and then follow-on with the quant or would it be the same rigor from the EUA application point of view to do both?

Timothy Stenzel: I think, you know, having a conversation, you know, through a pre-EUA exchange with our reviewers would be good in this space. It, you know, there is going to be more validation for - required for quant assay. And so if you want to, you know, sort of have an EUA authorization as quick as possible doing the semi quant first and following-up with the full quant may make a good strategy for you. But we're open to either.

(Jess Terivery): Okay thank you very much sir.

Coordinator: Our next question comes from (Trey Koshik). Your line is now open.

(Trey Koshik): Good afternoon Tim and Toby. Thank you very much for these calls. They're very useful to us. I just have one question to Toby which revolves around the template for the non - I can't remember the name but the non-facility use. We are in the process of actually writing a pre-submission that - or sorry the EUA to - so that a university or, you know, let's say Amazon or Walmart could sort of run samples of their employees coming in and, you know, and then make call of saying, you know, whether they have COVID or not and to send them home.



The question I have is for some reason I thought that the new template was applicable. But so do we submit those on the regular molecular diagnostic templates for - by manufacturers?

Toby Lowe: So it sounds like what you're referring to would most likely be considered a point of care test where we - where an individual would provide a sample to someone at the facility that is performing the test and interpreting and returning the result.

In that case I would encourage you to look at the more general molecular diagnostic template for commercial manufacturers which includes the section on point of care testing. And we would then expect for those tests to be performed at a facility that is operating under a CLIA certificate. Typically those would be certificates of waiver which are fairly straightforward to take out from (CMS).

The non-lab template is really for self-tests where there is no, you know, no need to install an instrument, no need for an individual or for personnel at the facility to be interacting at all with the test.

Timothy Stenzel: Now...

(Trey Koshik): Would you...

Timothy Stenzel: ...let me just ask a follow-up question. Is the environment you're looking at going to have a CLIA certificate, a CLIA - or a CLIA waiver certificate or are you looking at situations outside of a CLIA waived lab?

(Trey Koshik): No we're looking at outside a CLIA waive. So let's say a school decides to do

this in their nursing room basically to test every kid that comes into the school. And that if the fever and other symptoms if it turns out that they come up to be COVID positive and they will be sent home and their test would be confirmed with a CLIA waived lab on the back end. That - I mean, it's not going to be like a doctor's office for a CLIA waived setting like CVS or something of that sort. It's going to be more the general population.

Toby Lowe: Right, we'll...

Timothy Stenzel: Yes, so for diagnosis...

Toby Lowe: Go ahead.

Timothy Stenzel: All right. For, you know, diagnostic or screening situations outside of a CLIA waive environment I'll just add a little bit more color to what Toby already has said about the non-lab setting. It can absolutely be a test that can be performed by a consumer or if it's prescription by under prescription by the individual outside of a lab setting.

There's going to be situations where that need some of these tests may be authorized for testing kids and so, you know, a guardian or a parent or another a person given permission by the guardian or parent to administer the test outside of a lab situation we'll be considering those populations and those authorizations. So that - in that case it's not the person doing it on themselves but it's the person doing it on a child who's not capable of doing it on themselves.

And we've looked at the safety situation there as far as the actual sample collection and all the reagents that are with the test. But to expand that there will be situations in these non-lab settings like workplace, obviously home, school.

So this is really anywhere there's not a - going to be a CLIA certificate available.

And we do want to make these tests available in those settings as well both by prescription and by over the counter. And the non-lab template is for - what it sounds like as long as you're going for screening or diagnostic indications is a good one for you to look at. And it is just to add color to what Toby said it can be outside of the home environment as well.

Toby Lowe: Right and just to clarify, it can be outside of the home environment as Tim said. If it is, you know, in a school we do have, you know, we have had discussions with the CLIA program at CMS and they do provide CLIA certificates of waiver to schools. They have programs in place to do that, you know, on a broad, you know school district level for example.

And if it is a situation where, you know, as you suggested perhaps the school nurse is providing the test and performing the test, that is a situation where CMS would expect the school to have a certificate of waiver to provide that testing. But if it is a situation where the individual or perhaps or their parent or guardian is performing the testing without the assistance of a personnel from the facility that would be - that would fall under the new non-laboratory use template.

Trey Koshik): So right and let's - and let's take the school nurse out but well let's say it's in the local Walmart they're - they probably have a small pharmacy and I know the pharmacy can probably run these things and on site. So I would assume even those would be required to have a CLIA waiver certificate...

Toby Lowe: Yes. A lot of pharmacies do have certificates of waiver from CLIA and if they - if the personnel at that facility at the pharmacy are assisting in the testing then, my understanding from CMS is that they would expect the facility to have a

CLIA certificate. If they are simply providing a self-test that the individual performs on themselves and interprets themselves then the facility would not need a certificate.

Trey Koshik): And the question would - still comes back to the temple because in my mind that that tells me that, you know, depending on where it is, we have to submit two different templates. One is the point of care and one is the non-traditional use templates. Is that correct? Am I interpreting that correctly?

Timothy Stenzel: So...

Toby Lowe: You can take portions from...

Timothy Stenzel: ...let me just...

Toby Lowe: Oh go ahead Tim.

Timothy Stenzel: Yes, I was going to say if you're just going to reserve yourself to launching a test in a CLIA waived or moderately and/or high complexity because anything that's CLIA waived can be run in modern the complex or high complexity labs as well. However if you want to go to these self-test situations that - and Toby just went through you'll want the non-lab.

And when we authorize - and Toby I hope this is correct, when we authorized a non-lab test for use. the self-administered it automatically is CLIA waived as well. So it can be run in a CLIA waived setting and performed by a health care worker.

Toby Lowe: Right that's correct. And we would typically if we were authorizing a test for, you know, self-testing we would probably - we would work with the developer

to make sure that there are appropriate instructions for use in the package insert so that a healthcare provider can also perform it in a certificate of waiver setting under the instructions for use without deviating which is the regulation for certificate of waiver laboratory. So and regarding...

((Crosstalk))

Toby Lowe: ...the template in particular you don't need to submit two templates. If there are things that you see that are relevant to your particular situation that are in each template you can combine them. You can pull the parts that makes sense for your situation...

(Trey Koshik): Yes.

Toby Lowe: ...into one document

(Trey Koshik): Yes thank you very much. That answers my question. Again you guys are doing a fantastic job. I just want to - I really appreciate the time that you're spending to explain these to us.

Toby Lowe: Sure, glad it's helpful.

Coordinator: Our next question comes from (BJ Tatel). Your line is now open.

(BJ Tatel): Hello. Thank you for taking my question here. My question is for CDCs multiplex combo flu and SARS CoV-2 assay. I know it's pretty early and they are probably working on all the logistics and whatnot. I was just trying to get a feel for how FDA is helping CDC to launch these to the private labs. I think there's a path for all the public labs and other one through IRR but for private lab I would just want to understand if they are going to launch it like the

previous version or there's going to be any difference from the FDA's point of view?

Timothy Stenzel: I can start and Toby you can finish. One thing is probably talking to the CDC would be a great thing to do. And Toby do you have any additional information to provide about this question?

Toby Lowe: Yes absolutely second that talking to CDC would be a great first step. I can tell you that, you know, from our discussions with CDC they are absolutely in encouragement of laboratories to develop multi analyte tests like this and they are putting out information about their test to encourage laboratories to use it as the basis for new tests. And they are providing right of reference to other laboratories to use the information in their EUA similar to what they did...

Timothy Stenzel: Yes.

Toby Lowe: ...for their single test.

(BJ Tatel): Okay, thank you.

((Crosstalk))

Timothy Stenzel: So if you follow that pathway you would do your own validation of that test. And then Toby is there, you know, you would you would order your own primers and probes and reagents and validate it. But Toby do you have any other further recommendations for what they do with that data?

Toby Lowe: Yes, we would want you to come in with an EUA request for your test. But you could in your EUA request reference the CDC EUA so you would not have to repeat the validation that they have in their EUA. We could leverage that.

(BJ Tatel): Okay so you guys definitely want an EUA submission?

Toby Lowe: Yes that's kind of their expectation.

(BJ Tatel): Okay great. Thank you.

Coordinator: Our next question comes from (Annie Bell). Your line is now open.

(Annie Bell): Hi. Thanks for taking my question. I have a two-part question related to the antigen template. The first...

Timothy Stenzel: Sure.

(Annie Bell): ...being - sure okay, that the population for the non-laboratory template says that the population can be enriched is - but it does not say that in the healthcare setting template. Can the population be enriched to include those who test positive in either non-laboratory or a healthcare setting?

Timothy Stenzel: Toby did you catch all that? I could use a going over that question again because It's a fairly detailed question on what's in our template. I just want to make sure I capture your request.

Toby Lowe: I think they're - I think the question is whether the data for your study can be enriched for point of care tests for antigen the way that in...

((Crosstalk))

Toby Lowe: ...for point of care the way that it is noted in the non-lab template. Is that the question?

(Annie Bell): Correct, exactly.

Toby Lowe: Yes, we would - if you can send that question in so that you can talk with our antigen team about it, that would be the best step. Generally yes, we would consider that to be a reasonable approach but we would want to discuss the way that you're doing it. And we will most likely be updating the antigen template to include information on that.

(Annie Bell): Okay so that was my second part to that question. It says that enriching including by another assay and I was curious if there's limitations to the assays that can be used to confirm a positive case?

Toby Lowe: I think that probably would be a better question to discuss with our antigen team specifically but generally you'd want to use a high sensitivity PCR test as a comparator.

(Annie Bell): Okay all right. Thanks for your help.

Toby Lowe: And - yes and regarding enriching I know that the team also wants to consider how you're addressing bias if it's the test that's visually read.

(Annie Bell): Sure. Understood. Thank you.

Toby Lowe: Sure.

Coordinator: Our next question comes from (Robert DeTullio). Your line is now open.

(Robert DeTullio): Well thank you very much for allowing me to have the question and thanks again for all the work you guys are doing during this pandemic -- appreciate it.



My question is around the triage program. So I understand that because of the large number of submissions there's a - kind of a waiting period for certain tests that are submitted before they're assigned to a reviewer. And I'd like to know a little bit about the process of assigning it into the triage and how to get it out, please?

Timothy Stenzel: Yes, I can take a crack at that and Toby can fill in. So are our reviewers are obviously their desks and plates are very full with submissions and reviews. And in order to get through them as quickly as possible we have a program that when we receive an application we want to make sure it's not something that requires an EUA to launch that is if there's a notification pathway for the test and/or it doesn't have - it meets one of our other definitions for something that would be put into a high priority category.

And then if it doesn't meet any of those categories and perhaps even if it does if our reviewers' plates are full, there is a triage program or I wouldn't call it triage. There's just a program that puts applications with somebody who can keep in contact with the developer and give them a status update at least on a weekly basis as to where their application is in the process.

And as soon as a space opens up on reviewers' plates then we put in those submissions based on the kinds of priorities that I discussed onto the next open reviewers' slot that they are carrying a number of applications all at once and then the beginning of a true interactive review can happen. So typically those happen for tests that can be launched through the notification pathway prior to an EUA authorization. I'll pause there in case...

((Crosstalk))

Timothy Stenzel: ...you have any follow-up questions.

(Robert DeTullio): No I - yes, I do. That's actually very enlightening. Thank you so much for that. So but the notification process for a test that allows someone to announce that they have the test in the world doesn't carry the same weight as being able to announce that this is an EUA authorized test. So is it strictly based upon let's say the CDC categorization of how a test is going to be used or is there some other method?

Timothy Stenzel: Of determining priorities?

(Robert DeTullio): Yes.

Timothy Stenzel: So, you know, anything that's the point of care if it's truly going to be used at point of care does require an EUA authorization to deem it as CLIA waived or non-lab or home collection situations. So those all require EUAs and so they aren't allowed to launch for those indications until they have that EUA authorization. So those are the ones in greatest need to be able to offer that test in the US. So those and those do get a higher priority because of that requirement.

So if all the point of care test information is in the application for the reviewer to review then they would receive - that would receive a higher priority in our review process because they can't notify and launch point of care.

(Robert DeTullio): Okay great, great. So in other words I think what I heard is if I have a point of care test, especially a rapid test it gets higher priority then I have something that can be launched in a high complexity lab. Is that right?

Timothy Stenzel: For which you can launch and market the test already. It's...

(Robert DeTullio): Yes.

Timothy Stenzel: Yes. And if you come in with something that that truly does, you know, with data that does require an authorization to be in that particular patient or consumer setting then - and can't just be performed in a high complexity lab, then that would automatically be a higher priority.

(Robert DeTullio): Great Tim, thank you very much and again a shout out to all of you. Thank you very much.

Coordinator: Our next question comes from (David). Your line is now open.

(David): I have a question about serology under the notification pathway and it's based on the self-testing discussed before. Could you go on with that? In a notified serology test using blood as a sample that the person taking the sample does not have to be an employee of the lab but that can be a phlebotomist or a clinician at a doctor's office as long as the lab is the one performing the test and interpreting the results. So my question A is about a sample that was taken from whole blood from a blood draw and Question B is a finger stick.

Timothy Stenzel: So a finger stick is something that I don't believe we have authorized sort of a finger stick method in an EUA authorization where you could transport that with a device. I don't - and Toby you can correct me, I don't think we have.

But as far as transporting and collecting somewhere else, transporting a serum plasma or whole blood sample if the test has been authorized for those sample types to a lab setting that has been authorized or allowed by our guidance in the notification process which in most cases of course is a high complexity lab, the testing can then be performed with that sample collected somewhere else in the high complexity lab.

(Robert DeTullio): But again the sample doesn't have to be collected by a lab person. It can be collected by anybody qualified to collect a blood sample.

Timothy Stenzel: That's my understanding. I'm not quite sure if that's fully an FDA question Toby do you know that?

((Crosstalk))

Toby Lowe: Right. My understanding from my colleagues at CMS is that CLIA generally does not require a CLIA certificate for a specimen collection only site. So at the collection site that does not need to fall under the laboratory and does not need to be staffed by lab personnel. Although I believe that some states may have more strict interpretations than the federal CLIA regulation.

But generally when we are referring to, you know, healthcare provider observed or directed or performed specimen collection as we've noted on a number of authorizations we would we would expect that that individual be someone who, you know, is generally trained in patient care but not necessarily trained in laboratory testing. But it would, you know, be someone who is licensed by whatever state or the local laws are necessary for specimen collection.

Timothy Stenzel: So from an FDA perspective, things should be clear from our - from the, you know, from the instructions for use that the testing is performed in the right setting. But sample collection is not so much unless we specify it under our purview. And so, you know, also perhaps going to CMS and checking on this would – or CLIA, would be and your state and local officials would be a good place also to check. Did we lose (David)?

Coordinator: Our next question...

Timothy Stenzel: Okay go ahead.

Coordinator: Our next question comes from (Louis Perlmutter).

(Louis Perlmutter): Yes. Thank you, Tim, and (Toby). I have I guess a question about the direct antigen test. There was issues that you talked about before about the saliva and you mentioned something about inconsistencies. How did the Yale people and others get around this issue? That's my first question. And the related question is where could I find the EAUs accepted tests on the FDA page?

Timothy Stenzel: So I can take a first stab at that. So we do have an In vitro Diagnostics EUA Web page at the FDA so that you can search on those terms. I don't know if the slide deck has a link to this or not that's been shared with participants today.

Toby Lowe: Yes it should.

Timothy Stenzel: Okay, okay. And so that's where you can, you know, find all the information on what's authorized and what studies were done and what the results of those studies are. So it's either depending on whether it's a kit manufacturer or not it's either called an IFU, Instructions for Use on EUA Summary and in all the information is in there.

And so we continue to have cautions about saliva. The - and we have not been able to authorize some or that - or some that we're willing to authorize have limitations because the performance comparison to the ideal recommended sample type which is a nasopharyngeal swab.

We'll also be open to a mid-turbinate swab. We found if the studies don't

compare to those two that we can - we're unclear of the actual performance because saliva being such a unique respiratory sample type and having issues that frankly that we don't fully understand the science around about why there is such variability.

Now very clearly there's been a lot of different sort of methods that we've authorized and we think that more will be coming as well using saliva because when we're, you know, we're cautious we realize that saliva is a very important sample type especially as have we've greatly expanded testing...

(Louis Perlmutter): Right.

Timothy Stenzel: ...and it's putting pressure on swabs and transport media. And so we absolutely see utility in using saliva. So the recommendations we make when attempting to validate saliva and if you've already - if you're a lab and you already have an EUA authorized test, either your lab test or a kit that you're using, you can, the lab can validate saliva without an EUA submission.

It's only if you're going to go into the home collection type situation that - and other non-lab non-health care setting collection where EUAs is required for that particular purpose. But if it's going to be collected in a healthcare facility under an observation...

(Louis Perlmutter): Yes, right.

Timothy Stenzel: ...you know, then you don't need to submit. The lab that's doing that doesn't need to submit that data to the FDA. We welcome submissions but it's not required and it's - but in order to really demonstrate great performance we're asking for the comparator to be a nasopharyngeal or a mid-turbinate swab and also that a good distribution of virus levels be validated. So...

(Louis Perlmutter): Right.

Timothy Stenzel: ...for example if you were to load everything up with very high viral load samples...

(Louis Perlmutter): Right.

Timothy Stenzel: ...as measured by the swab that would that would tend to overestimate the performance of saliva portion of the test. and vice versa you don't want to overestimate very, very low positives because that puts the saliva sample type at jeopardy of not meeting an expected performance. So, you know, a good a normal sort of distribution from high viral load to low viral load on the swab sample is the way to go ahead and validate saliva.

(Louis Perlmutter): Great. Thanks very much.

Coordinator: Our next question comes from (Daniel Markus). Your line is now open.

(Daniel Markus): Hey guys. I can't - let me start by saying I can't tell you how excited I am that the topic de jour is point of care because I've got plenty of questions and I'll try to keep them brief.

So my first question is as to how you guys go about determining complexity of a point of care test or complexity such that you deem them to be sufficient to be deemed a point of care test simply because, you know, I've been (polemically) studying which tests you've designated to be point of care tests and trying to find the commonalities with that and reverse engineering them from the CLIA complexity score card. And I'm just wondering how you go about that and whether there are certain assay types that are more difficult to make a point of

care case for than others?

Timothy Stenzel: Yes so at a high level just to, you know, establish a baseline of understanding here, a point of care test should be easy to perform in a CLIA waived lab - a CLIA waived setting by non-laboratorians right, so anything that may require say precision pipetting or more advanced equipment that's not usually present or can't be provided in that setting. It - so it should be easy to perform. It should be something that also gives accurate results that can be easily read and easily interpreted okay?

And it does loosely - we do loosely if that - now, you know, consider the point of care checklist that you referred to. But one thing to make clear is that we are not - we are deeming the CLIA waived status with authorizations. We are not making a final CLIA waiver decision or CLIA category decision for a particular device. Once that device is converted to a normal submission and we make a decision through the normal 510(k) de novo pathways then the formal CLIA categorization will be applied to that.

One of the reasons for that is that we are - the bar here for sufficient clinical testing and performance is so much lower than our normal bar. And we want to make sure that when we make that final decision on the final device at conversion meets our CLIA performance considerations.

So if you look at what we've authorized already, some of them were on instruments that we have previously waived. And as long as the workflow hasn't changed that would introduce any more challenges to the point of care setting, we have not required additional point of care studies.

It's - but a device that has never been waived prior to the pandemic. We are asking for some very, you know, less - a lower bar as far as the amount of



validation goes for the CLIA waived setting to show that it can be easily and accurately performed and interpreted.

And that includes any steps that there are - that there's appropriate guard band studies I call them but basically flex studies that look at if you shift time of reading, time of incubations beyond the package insert what is the what is the effect on result.

So hopefully that's helpful. Those who are seeking point of care tests here we - you can come in with the pre EUA and ask specific questions about whether your device, you know, in development would potentially meet the criteria for that. And then of course we make that decision during the formal EUA review process. Toby did I...

((Crosstalk))

Timothy Stenzel: ...do a decent job of that.

(Daniel Markus): But my more specific question is well I guess here's a statement. The statement is you're right. I mean you guys had to authorize instruments that have already been existing have been authorized for use at the point of care. And the problem we have with supply meeting demand in this country is the fact that there's just a dearth of those instruments. And to be able to get enough of those instruments in the amount of time that we need to do it is a problem.

So my question specifically is whether you consider something like 96 well plate based assay, something that provided it perhaps -- and I haven't looked -- that you authorize such assay to be used at the point of care something that you would consider to fall within the bucket or the mold of what you would consider to be a point of care test.

Timothy Stenzel: Yes. So something that involves a 96 well plate usually involves precision typesetting something that a non-laboratorian would not be trained in. And I'm not going to say, you know, no until we see more details about a specific test. But it would be very challenging. Those lab environments are not set up to prevent cross-contamination, monitoring contamination -- things like that.

So typically these point of care assays need to be self-contained so that disposal is easy and doesn't result in contaminating the work area where the testing is performed. So I'd encourage you to come in with some ideas, absolutely interested in point of care. They are - I have had experience developing point of care devices. They are and getting moved to the FDA. And they are before I joined the FDA and they are a bit more challenging to develop. We understand that.

But you will see you will see more and more point of care tests authorized in this pandemic and hopefully in the near future that don't require instrumentation. So...

(Daniel Markus): is the bar higher in terms of validation for someone that wants to basically get their test through the point of care tests or is it comparable or even lower than, you know, a lab-based assay?

Timothy Stenzel: The percent positive agreement or sensitivity and specificities are basically the same that we would allow - we have authorized the direct antigen test. Some of them at least initially were say at the 80% PPA or sensitivity mark in carry. And some of them I think still do carry a presumed negative claim.

So, you know, we typically we think of a central lab saying molecular test as being able to do much better than an 80% PPA or sensitivity. But we do - we

have lowered the bar to these point of care devices as I mentioned sort of in the beginning of this call. If it's down to 80% for a point of care say direct antigen test and a molecular test we would authorize as well but there would be a limitation that the negatives might not really be negative.

And so we have lowered the bar relative to what normally people think of as a central lab test. And one of the reasons for that is identifying this population of patients that have very high viral loads that are likely to be infectious or they're symptomatic and you want to know right away in a point of care center setting do they, you know, are they positive? So unfortunately, I think we've - maybe we can sneak in one more question. I know we spent a lot of time with you but hopefully that you found that helpful.

(Daniel Markus): No I find it very helpful. Thank you very much.

Irene Aihie: Operator we'll take our last question.

Coordinator: Our next question comes from (Laura D'Angelo). Your line is now open.

(Laura D'Angelo): Hi. I want to well I think my question was a little bit already addressed. But just for clarity - and thank you for holding these. We find them deeply essential. So we know the backlog is still fairly significant. Your offices are prioritizing. You know, we're working on the triage program. But is there a limit as to how long a test can be out there on the notification pathway like without any kind of, you know, substantive review from you guys or authorization by the agency? No from my understanding.

Timothy Stenzel: Well there is no limit. And what we do when we receive applications is, we have our expert review staff take a quick look at it and they do a couple of really key things when they take a good look at it. First of all does it fall into one of

these higher priority buckets that requires or would benefit, public health would really benefit from an authorization coming sooner than later? And then second are there any issues that we see? And that is, are there any performance characteristics, issues that would suggest there would be any sort of risk to public health?

If there is that does get put into a higher priority bucket so that we can reach out to the developer and likely ask for some more information about what's going on. And, you know, and deal appropriately with the response that we get. And we have denied a number of assays that have fallen into that category already.

And we maintain some of that list on our Web site. So the other thing they - we want them to do is note if there's any missing pieces to the application. And then they give that over to the assigned contact and that contact can provide that feedback to the developer.

That is okay your application, you know, looks complete and we're in a holding pattern right now. And if you notified then you have confirmation of notification from us. That will happen. That doesn't have to wait on a reviewer. But also that contact can say, "Oh we took a look at it. We don't necessarily have many concerns at the moment but we noticed that you have these missing elements so that you can work on those."

And those can be provided because we actually probably in most cases won't hand that application over to a reviewer until we think that the application is complete so the reviewer's making the most efficient use of their time and as rapidly as possible reaching authorization decisions for the items that are on their plate and they're not holding in holding patterns with a number of different developers. So hopefully that's helpful and answers your question.

(Laura D'Angelo): It kind of does.

Toby Lowe: It's Toby. I just want to jump in with one quick point to follow-up on some things that Tim just said. I just want to remind everyone that when you submit an EUA request that is not the same as a notification. You don't need to necessarily send a separate email but you do need to specify in your email when you send in your EUA request if you are also notifying. If you do not specify that you are providing notification then we will not consider you to be a notified test and we will not put you on the list as notified tests.

(Laura D'Angelo): Thank you so just point of clarification, I know we're definitely out of time, but after a test has - after theoretically we've submitted a test for notification and, you know, the triage kind of reviewer sees that we are missing some element will we at that point receive a confirmation of notification while working with our point of contact to kind of flush out the application or will we not receive a confirmation of notification until, you know, kind of all it's administratively complete?

Timothy Stenzel: Well if we see any elements that are missing as called out in the guidance as far as what's allowed via an allowed notification option, we would work with you on that to make sure that those things are - have been validated for example. So if there's clearly something missing like, you know, there's no - but again the notification process can happen before the submission right.

So we're - this is the honor system that you notify us that you've validated your test and then you have a certain period of time to submit the EUA. Once we get it then we will do a quick review to make sure what prioritization that gets and if there are any missing elements and if there is, you know, any concerns, public health concerns okay? All right I think we...

(Laura D'Angelo): Okay thank you very much.

Timothy Stenzel: ...probably want to close things out. Thank you.

Coordinator: We are now finished with our Q&A session. I would now like to turn the conference over to Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcripts will be made available on the CDRH Learn Web page at [www.fda.gov/training/cdrhlearn](http://www.fda.gov/training/cdrhlearn) by Tuesday August 25.

If you have additional questions about today's presentation please email [cdrh-eua-templates@fda.hhs.gov](mailto:cdrh-eua-templates@fda.hhs.gov). As 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](http://www.fda.gov/cdrhWebinar) immediately following the conclusion of today's lively discussion. Again thank you for participating and this concludes today's discussion.

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