

**FDA Virtual Town Hall Series –  
Immediately in Effect Guidance on  
Coronavirus (COVID-19) Diagnostic Tests Moderator: Irene Aihie  
September 2, 2020  
12:15 pm ET**

Operator: Welcome and thank you for standing by. At this time, I'd like to inform all participants that today's call is being recorded. If you have any objections you may disconnect at this time. You have been placed in a listen-only mode until the question and answer session of today's call. At that time if you would like to ask a question, please press star followed by one. Please make sure that your phone is unmuted and record your name when prompted. Please allow yourself one question and one follow up. Questions will be taking -- be taken over the phone only.

I would now like to turn the call over to your host, Ms. Irene Aihie. Thank you, ma'am you may begin.

Irene Aihie: Thank you. Hello, I'm Irene Aihie of CDRH's Office of Communications and Education. Welcome to the FDA's 24th in a series of virtual town hall meetings to help answer technical questions about the development and validations 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 in 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 lines for your questions related to today's discussion. Please remember that we are not able to respond to questions about specific submissions that might be under review. Now I give you Timothy.

Timothy Stenzel: Hello, everyone, and thanks again for joining us today. We appreciate the dialogue that happens during these calls and the dialogue that happens in between these calls offline through our emails and other contacts.

We look forward to trying to help out again today. I wanted to just go over some remarks that I've made in previous public forums. First, regarding our templates that are posted on the website, we, first of all are working on a serology, non-lab or home collection template. And we're working on a serology home test or non-lab test template. And the progress there continues to go forward.

And then regarding the templates that are already posted, we have recommendations in there on validation. And we have given a lot of thought to those recommendations. So we feel like those are good starting points for discussion. However, they are recommendations and we are open to alternatives.

The other thing I wanted to make clear was for home use or non-lab tests for both molecular and antigen tests, we are very open to serial testing protocols in order to increase the PPA, or sensitivity of the essays. During the same period of time, that folks who have contracted the virus and are symptomatic, you know, in those first five to seven days or so, we really want to see good overall performance on detection of virus in that time

period. You know, and it would be a similar time period post infection for asymptomatic individuals.

But we really would like to see, you know, good performance on detection of virus positive individuals during that period, which generally correlates, if not completely correlates with the period of maximum infectivity risk. So that individuals will get tested, know if they're at risk of spreading SARS or not and they can take appropriate actions to protect those they may come in contact with.

And with that, I will turn it over to the operator for questions from callers.

Thank you.

Operator: Yes, sir. It is now time for the question and answer session of today's call. If you would like to ask a question over the phone, please press star followed by one. Please make sure that your phone is unmuted and record your name when prompted. Again, please allow yourself one question and one follow up. Thank you.

First question comes from (Greg). Your line is open. First question comes from (Greg Ping). Your line is open, sir.

(Greg Ping): Dr. Stenzel, can you hear me?

Timothy Stenzel: Yes, we can. Thanks.

(Greg Ping): Can you hear me?

Timothy Stenzel: Yes, yes, we can.

(Greg Ping): Thank you. The question that I have is, would the agency comment or are you concerned by recent antigen test EUA approvals where the sensitivity and performance was driven by samples that were obtained in high prevalence settings, you know, like greater than 30 percent. This doesn't really seem to reflect the national average of eight to 10 percent. So I would like to know your comments, please.

Timothy Stenzel: Yes, no, I appreciate the question. The prevalence of disease in a population for a direct antigen test probably doesn't have an impact on

performance characteristics, that is the sensitivity or PPA or the specificity and MPA. It does, however, allow developers of tests to which we fully support to more rapidly accumulate positive and negative information so that we can make a decision that much more quickly on tests and get those tests out there. So, you know, that's at least our view, but, you know, if you have specific concerns about that, I'd love to hear them.

(Greg Ping): So you would have -- tried to narrow our inclusion criteria to include people that had a couple of different symptoms instead of maybe just one or two.

Timothy Stenzel: So, yes. So when it's easiest for us to make a determination on how good a test is, if we get data per patient, you know, how many days since they began having any symptoms. We don't necessarily prescribe on what those symptoms are. But, you know, symptom onset for those who are symptomatic is a good indication of the course of the viral infection, and gives us a clear indication of, you know, sort of what we kind of expect the detection rate to be in those patients by day after the beginning of symptoms.

So some of the direct antigen tests have either presented data only in the first five days or seven days or have had a decrease in performance potentially after five days. So -- and then we want, you know, a good molecular confirmation that those patients, you know, have SARS so that we have a, you know, a good comparator upon which to base whether a patient is either positive or should be positive or negative for the virus. Hopefully that helps.

(Greg Ping): Thank you.

Operator: Thank you. Next question comes from Shannon, your line is open.

Shannon Clark: Hello, this is Shannon Clark, CEO of UserWise Consulting.

We're experts in recruiting and conducting human factor studies in different languages such as Spanish. My question is that the non-lab template notes that we need to recruit Spanish speakers as part of the human factors study of the Spanish IFU. In the studies we never asked you to please follow the instructions. So it's really up to them whether they follow the English or Spanish IFU. So if Spanish speaker choose to use English ICU while they're using the product and then we assess them the understandability of Spanish IFU after conclusion of using the product, is that acceptable? Or would you

prefer that we actually ask them to please switch over to Spanish IFU in the middle of their interaction with the product?

Timothy Stenzel: So, you know, inclusion of Spanish IFU instructions is something that we support. I don't believe it's a requirement. Toby maybe you can confirm. But English is a requirement and we definitely want to assess, you know, the English language version of the instructions. So, that would be important to have, you know, as some of the users perhaps English only speakers will be in the human factor so that we are assessing the English language version of the instructions.

Shannon Clark: Okay. So it's acceptable. Is it a requirement but that is interesting. it's in the template that we need to recruit Spanish speakers, which seems to imply that Spanish IFU is required?

Toby Lowe: The template is recommendations. So, if you have different approaches, you're welcome to bring those on.

Shannon Clark: Okay, thank you.



Toby Lowe: Sure.

Operator: Thank you. Next question comes from (Louis). Your line is open.

(Louis): Yes, I just want to ask the question, of course -- this is Dr. (Venus), pushing the concept for the direct antigen test. And I guess I want to know if there's, you know, has been more test submitted and approved for saliva base and where can I find them if they have?

Timothy Stenzel: So you're asking if -- do we -- have we authorized the saliva base direct antigen test?

(Louis): Correct.

Timothy Stenzel: And that would be, no, we haven't. Though we're open to it and discussions with various developers of direct antigen tests they haven't necessarily taken us up on that. And there may be good reason. I personally have not seen performance data of a direct antigen test on saliva as compared to traditional, you know, swab sample from the nasal passages of some sort for a molecular competitor.

(Louis): Right.

Timothy Stenzel: But if the performance is good, can be demonstrated we're open to that sample time.

(Louis): Yes, I'm hoping there'd be some home tests as well. You know, within that framework, because that would really complete the exercise.

Timothy Stenzel: Yes. Well, you know, if a test platform is whether direct antigen or molecular is amenable to a swab type sample either direct swab or swab into a media before it goes on to the test.

We already know that because of the home collection authorizations we've made for swabs that self collection in the home, unobserved, with the nasal swab works very well. So that is an option, be at swabs can be in short supply as well as media, obviously.

(Louis): Okay, thanks very much, Tim.

Operator: Thank you. Next question comes from (Suzanne). Your line is open.

(Suzanne): Hi, thank you, but my question was actually already addressed.

Operator: Okay, thank you. I will go to the next person. And that question comes from (Susan). Your line is open.

(Susan): Thank you.

Operator: (Susan), your line is open.

(Susan): Yes. My question was already addressed. Thank you.

Operator: Thank you. Next question comes from (Sue). Your line is open.

(Sue): Hi, this is (Sue). Thank you, again for having these calls each week is really helpful. And, you know, I know and I've learned over the past four months, you know, that the reviewers are under a lot of pressure and there's a huge workload and I'm just curious if there is a way that we could get a phone call with one of you to kind of just understand where we are. We do

have an antibody test and we understand the whole notification process.

However, our test does have features that qualify for more of a priority. And I mean, it's been over 100 days. And we also have a reviewer that's part time. So I think that makes it a little bit more difficult. And I guess my question is, I'm curious why if we have features that would qualify for more of a priority.

Timothy Stenzel: This is Tim, I'm happy to -- I'm happy to get into the weeds, the granularity on your submission. If you send an email to the CDRH-EUA-Templates email asked to be connected with me on your application. I will look into it and communicate with you.

(Sue): I really appreciate it. Thank you.

Operator: Thank you. Next question comes from (Jessica). Your line is open.

(Jessica): Yes, thank you. Can you -- hello? Do you hear me?

Timothy Stenzel: Hello, we can hear you. We can hear you. You are breaking up just a little bit. So go forward.

(Jessica): Can you just say a little bit more about what you said at the outset about serial testing protocols?

Timothy Stenzel: Yes. So if a particular test, there's been some discussion around say, you know, something that can be done daily with consumers or patients in the home to assess whether or not they're positive for the virus, obviously, probably more looking at asymptomatic carriers. But also people who are symptomatic and want to know, you know, I just talked to somebody who, you know, and they just have a common cold. Now we're getting into the cold and flu season. And symptoms don't necessarily, you know, don't tell you whether it's SARS or not especially if you're not, you know a patient is very, very sick.

And so we've had open dialogue with a number of groups around, you know, what the sensitivity of a single test result should be. And you know, if the sensitivity of a single test result is not say high enough for us to be able to be comfortable making the authorization for that test. It may be that if you test days one and two or days one and three. So you might provide the consumer or patient with two self tests. And it's the combined results that matters not

so much a single results. So if either one of them is positive, then that may improve performance of maybe a very widely available test, just to where we're comfortable.

And really, what we would like to see is that, you know, is that if a single -- you know, we all the direct antigen test that we've authorized so far, especially during the core period of symptoms, which correlates really, into a relatively high viral load. In the first five days, they all perform well above our recommended level for authorization. And so we're pleased to see that but we're open to other tests that may benefit from doing it in say twos. You know, do it day one, day two. Do it day one, day three, and if the performance overall, you know, is sufficient to justify authorization we're open to that. So hopefully that clears up that sort of serial testing option.

(Jessica): Yes, that's very helpful. Thank you.

Operator: Thank you. Next question comes from (Leonardo). Your line is open.

(Leonardo): Hi, good morning. This is (Leonardo) from (New Road) clinical laboratories in a CLS over here. My question is, with the issues of finding

steady supplies of swabs and media, I've noticed that there is a vendor that has been listed in four different new EUAs. We currently use the Thermo Fisher EUA protocol. And this one, EUA that came out, supports this media. I was wondering if any additional validation or if you guys have any advice on how to proceed if it were to bring this new media into our lab, which is a media that's not saline or regular VTM or UTM. And they claim to be stable in temperature for up to 21 days. So how would we -- How should we proceed if this media is listed in the EUA that uses our reagents and protocols in Thermo Fisher?

Timothy Stenzel: Okay, if I understand correctly, you're using the Thermo Fisher EUA test and you want to know if you can use the different transport media for that test, is that correct?

(Leonardo): Yes, transport media that was validated LOD studies done under a different EUA that uses the same reagent.

Timothy Stenzel: Okay. And this is, you know, collected -- samples collected by healthcare providers and sent to your lab, right?

(Leonardo): Correct. That would be the supervised on site, mid-turbinate sub-collection.

Timothy Stenzel: Okay, I think Toby's going to respond to this.

Toby Lowe: Yes. So generally, you would want to do, you know, the normal verification that you would do under CLIA to change the media that you're using. It depends a little bit on exactly what test you're running and exactly what the other media is that you're using. So it might be best to send in the specific details to the mailbox so that we can take a look but typically, you know, we do have some information on our FAQ about alternate media that can be used and, you know, has been validated and so that that technically is not something that would be a problem.

(Leonardo): Great. That's great. Awesome, so I'll submit the details. But thank you so much.

Toby Lowe: Sure.



Operator: Thank you. Next question comes from (Lynn). Your line is open.

(Lynn), your line is open. (Lynn Nedle), your line is open. Okay, we'll go to the next person. It comes from (Steve). Your line is open.

(Steve): Hi, good afternoon. My question is going to go back several calls. Tim you had mentioned again several calls ago that NCI was running around a 17 day average for testing and I'm seeing closer to about, we're at about eight weeks now. It's a just a general question. Can you tell me approximately what the average time is now? And if it's shifted more to other tests than just serology, obviously more tests than just serology test. What are we looking at right now?

Timothy Stenzel: Yes, so I'm just looking at the dashboard now and, it takes a minute, let me go back to it. The current average time of device receipt and NCI to generate results is 26 days. And the average time from the device receipt to public posting of that information, usually with the decision is 58 days. It does appear to be trending up on the time and NCI. So ...

(Steve): Sure. And I, of course, would expect that as you guys get busier and busier, it's going to trend up. Before it's, real quick, one follow up. Before it's posted publicly, the manufacturer would be notified prior, correct?

Timothy Stenzel: Absolutely, yes that's our standard policy, our standard procedure, but before we make anything publicly, on any decisions, we do have some sort of discussion with sponsors, developers. In this case, they actually see the results of the testing from NCI before we make a decision and before we posted.

(Steve): And if we're beyond that 58 days do you suggest contacting them or best ...

Timothy Stenzel: No, contact the FDA. So you can reach out -- if your device has been there for more than that 26 days at NCI you can reach out to me. You know, Timothy Stenzel to the CDRH-EUA-Templates email, along with relevant information so the team can get that for me, so that I can look up and find out and give you a status report.

(Steve): Great. Thank you so much. I appreciate your help.

Operator: Thank you. Next question comes from (Karen). Your line is open.

(Karen): Thank you. My question was answered related to the (GL) testing.

Operator: Thank you. Next question comes from (Beverly). Your line is open.

(Beverly): Thank you. I appreciate it. I was wondering, with the EUA with the reference testing for samples, does that have to be done by a CLIA certified lab?

Timothy Stenzel: The reference samples are inactivated viral FDA reference panel that we send to all developers. So you have a kit rather than an LDT, is that correct?

(Beverly): Well, we haven't moved that far just yet. We're trying to trying to figure out our testing. But for the clinical testing, when we take the samples and do it in our test, and then do it in the reference, does the reference tests have to be done by a CLIA certified lab or could we do it in our ...

Timothy Stenzel: No, as long as a EUA authorized. You're talking about the initial validation. So as long as EUA authorized test is followed according to the instructions for that EUA authorized test, if you're going to make any deviations from that, I would check with our review staff before you do that testing to make sure those deviations are Okay.

(Beverly): Okay.

Timothy Stenzel: The validations can be done outside of a CLIA lab as long as the testing is done correctly.

(Beverly): Okay, great. Thank you.

Operator: Thank you. Next question comes from (Douglas). Your line is open.

(Douglas): Yes, hello. I'd like to echo the other folks. Thank you, Tim and Toby, for these meetings. Much appreciated. My question is regarding the recent change in the guidelines from the CDC, that say that asymptomatic patients who have been exposed to a patient with SARS 2 do not necessarily require

testing. And I'm wondering in particular, if that would have any expected impact on your templates, especially for direct antigen.

Timothy Stenzel: So, no and any questions about the CDC guidance I would direct to them. But we continue to support that those tests who have received the EUA authorization or have gone down the notified pathway, whether a direct antigen or molecular test, if there's a clinical order, a prescription for that test, and it happened to be on an asymptomatic patient than more supportive of the lab performing the test and reporting out the results for that individual. If a test developer wishes to specifically have a claim for detection of virus and an asymptomatic, individual or population, then you know, if they want to go and promote their test for that, then we're very willing to work with the test developer according to the, you know, we urge you to follow the template recommendations, but we're open to alternatives in order to show that the test works well in the asymptomatic population.

So it has to do with what the developer wants to promote their test for if it's, you know, the standard promotion, and they can do that without testing in the symptomatic population and clinicians and place an order for that test. And we've not heard pushback from labs. You know, of doing, performing

the testing on that in the high complexity labs, at least. So, and we've addressed some of the other concerns that other labs have had regarding CLIA-waived testing, and we believe those have all been addressed. So hopefully that answers your question.

(Douglas): Yes, thank you very much, Tim.

Operator: Thank you. Next question comes from (Josh). Your line is open.

(Josh): Hi, Tim. This is (Josh Dan). Thanks for taking my call. I have a question on behalf of the company and hopefully, the question involves when to escalate a communication. So if we've emailed the lead reviewer, and not received a response, is the next escalation, the reviewers not in microbiology, but the next escalation step be to CC that person's branch chief? Or is there a particular person they should speak to if we're not getting a response?

Timothy Stenzel: Yes, if you're not getting a response, and, you know, I would say that they're all very busy so. But you should be getting -- if you're in the

interactive review process with the reviewer, you should expect the communication back within 24 to 48 hours.

(Josh): Okay.

Timothy Stenzel: You know, unless it was the large amount of data and they need to, you know, plow through that. And you're always welcome to include other folks at the FDA on these emails. Hopefully, our reviewers are now and we're encouraging and taking some well deserved time off so that they can maintain their edge and being able to stay proficient or they should have an out of office message with another contact but barring that, if you're not getting a timely response, please take it to the team lead. So every reviewer has a team lead and then there's the branch chief.

(Josh): Okay, thank you.

Operator: Thank you. Next question comes from (Alexander). Your line is open.

(Alexander): Hi, thanks. I had a question regarding some of the prior enforcement actions that have been taken by your office. And I'm specifically thinking

back to one that happened on I believe, July where FDA indicated that there were certain laboratory tests that had been reviewed by the FDA and FDA, according to statements, determined that there were significant problems and warn the public against their use, I believe is Chemisys and Mayo Clinic Arizona.

My question though, relates to kind of backward enforcement and forward enforcement as relates to LDTs under the new HHS policy. Is your office kind of one, as relates to prior enforcement actions, does your office believe that it can still kind of warn folks against the use of particular test and two on a kind of ongoing or prospective basis. What does enforcement look like from OIVD against certain COVID tests that FDA believes may not be effective or safe or adequate for use?

Timothy Stenzel: Yes, no, that's a great question. I think Toby is going to respond.

Toby Lowe: Yes, so you're basically asking, you know, sort of what our processes for when we determine what to communicate in terms of the sorts of safety issues, is that correct?



(Alexander): Yes, or even more basic, you know, what are the new rules of the road for enforcement for that decision?

Toby Lowe: When you say, for that decision, what are you referring to?

(Alexander): Sorry for the HHS communication I suppose two weeks ago now that FDA had limited authority over LDTs to open some, perhaps.

Toby Lowe: Right. So I think, you know, Tim mentioned last week on the call, that we weren't necessarily commenting on that statement on that call last week. And I think that, unfortunately, we're still not going to be commenting specifically on that statement today.

In sort of more general terms, when we are determining what to communicate about a specific test, we look at what the safety implications are, the public health implications, based on the information that we have on hand and then we put out information that is available to be publicly distributed. And we put out that information that we think is necessary for

healthcare providers or laboratories or patients, the appropriate audience to be aware in a specific situation.

(Alexander): And one quick follow up if I may. Is there an expected timeline as to when your office believes that it may provide more information on the reactions of statement weeks, months?

Toby Lowe: I'm not able to provide that at the moment.

(Alexander): Okay, thank you.

Toby Lowe: Yes.

Operator: Thank you. Next question comes from (Kodamodi). Your line is open, sir.

(Kodamodi Vanakatesh): Good afternoon. Thanks for taking my call. I'm (Kodamodi Vanakatesh) from Tetracore. We have submitted our test to The NCI for evaluation more than three months. We haven't heard anything

from them. Is there anything that we can do? How we can get the NCI test results?

Timothy Stenzel: Yes. I'm not at liberty on the call to give specific questions and answers to that. But if you email, our CDRH-EUA-Templates email address and asked that, to Timothy Stenzel interact and then it should provide, you know, appropriate details in the email so that we can quickly identify you and email you and the information you'd like. And I will make sure that you get a response.

(Kodamodi Vanakatesh): Thank you so much. Yes, have a good day.

Toby Lowe: We'll take our next question.

(Kodamodi Vanakatesh): Thank you. I think my question is over.

Toby Lowe: Operator, are you there? Operator, are you there?

Operator: There are no further questions in queue at this time.

Timothy Stenzel: Okay, we can pause for a minute or so and if there are no more questions, we can close the call.

Irene Aihie: Thank you, was that the operator that spoke?

Operator: Yes, ma'am.

Irene Aihie: Okay, is Alexander Gaffney available?

Operator: He did ...

Irene Aihie: I see his name on the queue. I'm sorry, I can't hear you.

Operator: He did ask his question.

Irene Aihie: Okay.

Operator: He's not in the queue now. There is another one please let me get the name.

Irene Aihie: Thank you.

Operator: Next question comes from (Lynn). Your line is open.

(Lynn): Hello?

Timothy Stenzel: Hi, (Lynn).

(Lynn): Hello, can you hear me?

Irene Aihie: Yes, we can hear you, (Lynn).

(Lynn): Yes. Oh, yes. I'm so sorry. Yes. I missed the earlier part. So anyway, yes. So I have a question for the saliva molecular testing in comparison to NP so we're validating this. Does FDA have more data, like a viral shedding kinetics in saliva compared to NP. So I suppose to know, what is the best time to use saliva, you know, to test the -- to do the molecular test in comparison to NP?

Timothy Stenzel: Yes, that's a great question. Unfortunately, our knowledge about viral shedding into the saliva oral fluid is still being developed. traditionally with a respiratory virus NP swabs have been sort of the gold standard for collection. But for a variety of reasons and this pandemic, you know, saliva has taken on an interesting and important role.

We have seen quite variable performance with saliva. And in some cases, we're not able to authorize it or requiring more data in order to support an authorization. We're not sure. We're still gathering information about that. However, in a normal distribution of results with an NP swab or a mid-turbinate swab. In normal distribution, I would talk about, you know, there's a good variety and the normal sort of variety of the levels of positivity in the midturbinate swab or the NP swab, including, you know, we would say about 25 percent for a molecular test for saliva, that seek EUA authorization for saliva, that about 25 percent of those should be low positive.

We generally describe low positives as CTs that are over 30, but it does depend on the comparative molecular testing you're using. And we've found that assessment allows us to assess whether that particular saliva collection

method and the associated test that goes with that, and we can assess the quality of that test and make a determination.

(Lynn): Yes, Tim, thank you. Yes, actually, to follow up this center talking about those lower viral load like higher CT, and I actually have a question here. Usually when we determine the LOD is like at that level where 95 percent at least the next positive or the positive agreement or the detection. So, in that case for example, if the LOD like copies, real copy one, usually the CT of that value is not the cutoff value, right? But if the cutoff is 40 then we are -- LOD is around 36 or 35. I noticed that in many EUA like there's kind of a gap between the LOD and the cut off CT. So, in these cycles, in this gap, then there are naturally you will miss even with the NP itself, right, because of the spillover, the LOD.

In that sense, when you compare two ranges, that comparison when we compared to the other tests, or the saliva or something in that range, it's going to be -- it's not going to be good anyway. The NP itself is not reproducible to the extent. Is what that mean? Is that better to use the CT or cut off or it's better to use LOD as conductor and one times or two times

LOD to determine to see you have a second percentages for our 25 percent of the sample should be on that?

Timothy Stenzel: Yes, I know there definitely is usually a gap between LOD and the cutoff. And we do take that into consideration when we look at the data and the range of data. Many molecular LODs are well above 30 cycles, you know, you mentioned 30, mid 30s. And so we do take that into account.

We also take into account, you know, the test is, you know, is sensitive or not. And we've been sending out the FDA inactivated virus reference panel, and that's helping us begin to assess the relative sensitivities. So it's interesting that we do see some tests that have an LOD of around 30 cycles. And we definitely in those cases, certainly want to understand the relative LOD of those essays using the FDA only reference.

(Lynn): Okay, yes. I'm sorry if I can. May I asked one more question. I know there's nobody behind me. So I just go on the side.

Timothy Stenzel: There may be more now. There may be no one, so one more. Okay.



(Lynn): Okay. Thank you. Thank you. So the purpose about the CDC EUA test, so we use this as a competitor, right for our own test, and depends on, I think it's the RTP mix reagent. I did notice that there's some reagents probably a little more sensitive than others or for whatever reason. So I guess my question is, like, I want to talk to the FDA about a potential scenario where our test is actually a little more sensitive than the CDC. In that case, then our test would be labeled as false positive. So I'm kind of wondering here, how do you determine that the CDC test is the negative test, accurate a hundred percent and in every sense a little more sensitive than that is, must be false positive, so I'm just trying to -- what's the rationale behind that.

Timothy Stenzel: Yes, so you do bring up an important point, and then, you know, one that I've experienced prior to, in my development work prior to joining the FDA. So if you a more sensitive assay than the comparator asked you that you're using. How do you, you know, you make sure that you have false positives when you really don't, it's just that your assay is more sensitive.

So, you know, we do require that the comparator be EUA authorized now and then that can be, you know, it's best if there's no limitations on that assay, you don't want to pick an assay that that has low sensitivity and maybe has a presumed negative, you know, instructions for use right now because of potential low sensitivity.

But if there are no limitations, some of the limitations on the EUA authorize molecular test is a comparator, then, you know, you have the option of picking the comparator. And there are definitely a range of assays. And we are working hard to start posting some of the LOD relative LOD information on assays for those developers who have received the FDA panel and tested. So we think this is going to give developers and everyone in the testing community at least, you know, a better idea of what are the relative sensitivities of these essays?

Short of that, I mean, whatever comparator you have, we do -- there are options for how you can determine proof in that case. So you can you know, with FDA concurrency, you can have your plan, you can do a third test that might be more sensitive than the original comparator. And we can, at the very least, annotate the tables in the instructions for use with that

information showing that say, you know, another comparator that's more sensitive than the first comparator was also positive, just like what your essay ones, or if it was negative, and that information goes in the instructions for use as well.

And then there are ways to use multiple tests to establish truth usually that in both testing most of the samples with two tests. So, but there are different ways to achieve it when there are relative different sensitivities and it's our effort to help those tests that might be more sensitive than the comparator they're using.

(Lynn): Okay, yes. So to my understanding we are using the same primer probe as the EUAs, or an ((inaudible)) for example, if we're using the same then it's hard to think, or like you got false positive, you know, in a way -- it's a false positive. It's hard for me to imagine that way if the primary probe of the specific is high, is very high. It's kind of hard to imagine the false positive. Anyway, yes, thank you very much, Tim.

Timothy Stenzel: Okay.

Operator: Thank you. Next question comes from (Lee). Your line is open.

(Lee): Thank you for taking my call. Thank you for giving us the opportunity to work with you and hear from you directly. We know you're very busy but you have not approved any antibody test for a period of time. We wonder if now the antibody testing is at a lower priority. After you have like an antigen test, so that's my first question. Because we submitted our test to you a while ago to NCI for lab testing for more than three months, we haven't heard anything from you. And meanwhile, I want to ask your email, please spell clearly so that we can contact you. Thank you.

Timothy Stenzel: The email address, that should be posted on the slides that are with this meeting for reaching out, in this case, given that time period, I'm happy to look into it. So you can find me on Tim Stenzel via the CDRH-EUA-Templates@fda.hhs.gov email address. And I'll look into this specific situation again in the email to that address please, you know, give relevant information so we can quickly identify your application and we can look into the details.

(Lee): I'm sorry, can you repeat your email again?

Timothy Stenzel: Yes. CDRH-EUA-Templates@fda.hhs.gov.

(Lee): Got it. Thank you. There's so many emails so I'm not sure which one. So if that is possible that antibody test then now is the right lower priority after so long review. Because you haven't approved any antibody test lately?

Timothy Stenzel: Well, we approved two this week and we approved over the last few weeks we have. They remain important for us to authorize and when we have data supporting it, I would say that though, during that same period, we have denied more authorizations than we've authorized for serology tests.

(Lee): Yes. Thank you. So we're supposed to hear from you, either you approve or you deny, right? I mean, it should not be just no reply at all, right?

Timothy Stenzel: Yes. So we do move my directive that the contact you have, provide you at least weekly updates on the status of your application.

(Lee): Okay, one more suggestion. We submitted our tests to WHO as well. And they do have very good system that if you log in, you will see which stage

you are for your submission. And I think that might be something you can consider it. But I know that you're very busy. And we appreciate all of the hard work and the guidance you gave us. Thank you.

Timothy Stenzel: Yes, that's -- we've heard that suggestion before. And it's a very good suggestion. It does require, you know, an IT system that can support that. So, you definitely, that's definitely under consideration.

(Lee): Great, thank you very much.

Timothy Stenzel: But it won't happen, it has to ask with IT systems take a lot of work to get those.

(Lee): Yes, that's Okay. Just a suggestion. Thank you.

Operator: Thank you. Next question comes from (Griffin). Your line is open.

(Griffin): Hi, there. Thank you for taking my question. On the serial at home direct antigen tests you guys talked about earlier. Can you talk a little bit about what the data you'd be looking for there? In a submission I mean, I'm

assuming to real world asymptomatic population but then get some color on the number, you know, the size of the cohort, would it be larger than 30. And then in terms of performance of the individual test, that would be conducted serially to getting information you can provide there will be great.

Timothy Stenzel: So if we -- if you go to our non-lab diagnostic template is posted, it does go through the recommended positives and negatives for the study. If it is a by prescription test, you don't need to test any asymptomatic individuals. If it is an OTC, over the counter, non-prescription tests, then we do want to know the performance in the asymptomatic population because I know when you sell it to a consumer in the home, you don't know you know how it's going to be used, whether it's going to be in symptomatic people or asymptomatic. And they also on -- if it's not prescription, then they don't have somebody, they don't have a health care provider, helping them interpret the results.

And so when we talk about serial testing, think of say, like, it may be that it's a two pack. So two test in a package for one individual would, you know, be run on that individual, it just would be run on different days in order to try to increase the sensitivity for detection in that patient.

If a single test result with that device falls below our recommended levels, for example. So maybe, for example, you have a 70 percent single test result, but if you do two tests for the same patient, but it's on two different days and suddenly you pick up another 10 percent of positives, then you have that recommended 80 percent sensitivity.

Likewise, the specificity or MPA gets also tested twice. So you think of a device not as -- in this case not as a single test, but it's two tests together. Together, what is the sensitivity and together what is the specificity? I hope that helps.

(Griffin): That's great. Thank you very much.

Operator: Thank you. Last question comes from (David). Your line is open.

(David Rehberger): Hi, this is (David Rehberger). From BioFire Defense. We have an existing molecular EUA for testing NPS swabs and transport media. And we're looking into expanding this EUA to additional sample types. One of the sample types we're interested in pursuing is essentially just an NPS in



either sterile saline or sterile PDF. So we were wondering what types of additional testing would FDA require us to perform for that?

Timothy Stenzel: Yes, would this be clinician, a health care worker collected samples in a health care facility or a self collected under observation. Yes. Okay.

(David Rehberger): It would be health care.

Timothy Stenzel: Yes. So that is not a particularly challenging sample type. In order to include it in your label in your instructions for use in your labeling, yes we'd want you to validate that. That can be done usually with contrived samples using either live or inactivated virus is what our recommendations would be. You can still I believe get inactivated virus from the AI either radiated or inactivated. And we'd like to see typically near LOD work on mock samples. So you would spike in the normal patient matrix if its a nasal pharyngeal swab, taking a negative NP swab you would put it into your saline and/or your PBS and then you would spike that with take negative NP and we spiked that with near LOD, you know, around two x but I would check with our reviewers, LOD.

And I think they typically asked for 30 different samples. You can do that validation, you can send the validation to us as a EUA amendment. And then we're allowing you to go ahead and launch that change. Once you've submitted that amendment to us while we review that, if we have any questions, we'll reach out to you but we don't want to hold up, expanding your labeling and that way once you've completed the validation and submitted that validation needed to us.

(David Rehberger): Great, thank you.

Operator: Thank you. I would now like to turn the call back over to Ms. 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 CDRH Learn Webpage at [www.fda.gov/training/cdrhlearn](http://www.fda.gov/training/cdrhlearn) by Thursday, September 10. If you have additional questions about today's presentation, please email [CDRH-EUA-template@fda.hhs.gov](mailto:CDRH-EUA-template@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 live discussion. Again, thank you for participating and this concludes today's discussion.

Operator: That does conclude today's conference. You may disconnect at this time. And thank you for joining. Have a great day.

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