

**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 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 Communication. Welcome to the FDA's 15th 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 the 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 in 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 Toby.

Toby Lowe: Hi everyone. Thanks Irene. So I just have a quick update today. We put out a couple updates to the FAQs last week. I believe they went out on Wednesday but I think it was after the town hall so I don't think I mentioned it. If I did and this is a repeat sorry about that. So the first question that we updated last week was the question about current validation study recommendations. And we updated that question to clarify that the recommendations for testing apply - the FDA's recommendations for testing apply both to tests for which an EUA request is submitted as well as tests that are claiming to be validated and offered under the policies in the guidance prior to submission of an EUA request.

So those recommendations for validation are included in both the guidance and the accompanying EUA templates. So we encourage developers to consult those documents for those recommendations. And then the second question that we updated is the question on modifications to a previously authorized test. And the update in that question was to clarify a couple of points. The first is that modifications that are done by a high complexity CLIA Certified Lab under the policy in the guidance when we don't expect an EUA it does come outside of the scope of the EUA and therefore those tests are being offered as non-authorized tests.

And then the other clarification was to point out that we have two different policies regarding modifications. One is for tests that are modifying to add a new specimen type. And the other is for all other types of modifications. And we're pointing out that for new specimen types the guidance does not include

validation using a bridging study. So that type of modification we are encouraging developers to reference the information in the guidance and the templates regarding recommendations for validation of a new specimen type.

So those are all my updates for today.

Timothy Stenzel: All right. Thank you Toby. This is Tim. Welcome this week to our town hall. I don't have that many updates. In fact I just have one important announcement to make. We have noticed a spike in complaints about one of the newest authorized molecular tests. It is the BD SARS-CoV-2 reagent for the BD MAX System. There are two sets of reagents that are authorized for the BD MAX System. This is only one of them and this announcement only applies to the BD SARS-CoV-2 reagent. It does not apply to the BioGX SARS-CoV-2 reagents.

The new spikes in the complaints that we saw and have seen concern potential false-positive results. This appears to be a low level of approximately 3% of the overall positive results. So this is a small subset of the BD MAX positive results for this assay. For the time being out of an abundance of caution we are recommending that a positive result with this assay be treated as presumed positive and that you act accordingly when you are doing readings.

So we are working closely with BD, very interactively with them to establish what the root cause is and what the correction will be and what the validation plan for their correction will be. Stay tuned for additional announcements which is incoming in the near future with more details about what to do about this. But for the time being please treat positive results as presumptive positive.

And with that we turn - open this up to questions. Thank you.

Coordinator: Thank you. If you would like to ask a question please unmute your phone. Press Star 1. And record your first and last name clearly when prompted so I can introduce you. If you wish to withdraw your question press Star 2. Again to ask a question press Star 1. It may take a few moments for questions to come in. Please stand by.

And our first question is from (Ludna). You may ask your question.

Timothy Stenzel: Hello.

(Ludna): Hi. Can you hear me?

Timothy Stenzel: Yes.

(Ludna): Hi Tim. This is (Ludna) from (Hanson). I just wanted to ask about home diagnostic template if we - I know you've mentioned that you're working on a template for a true at-home molecular diagnostic template. I'm wondering where we are with that. And also in terms of at-home use products can be sort of true over the counter and they could also be prescription use. I'm wondering what your thoughts are on that and if we have an estimation for a template. I know you guys are working really hard. And I know it's a long weekend coming up. So I appreciate all the work.

Timothy Stenzel: Yes. So thanks for that question. So we're very open to home testing not just for molecular but also a rapid antigen and serology tests. We are in the, we are finalizing the home testing template for (unintelligible) molecular and direct antigen tests. And we hope to get that out shortly. In the interim if you want to send an email to the template's email address and we will at least put your name and contact information on a list as that becomes publicly available. We

plan to send that out to a number of folks as soon as that is finalized.

So yes. We are open to both prescription home use and to OTC. We call it prescription home use because it does require a prescription by a clinician to be able to offer this test. And we call it home even though we believe that this will be outside of a healthcare center and so it can be deployed in many different settings where there are not necessarily healthcare providers. So this could potentially be deployed readily at home but in other places such as schools and workplaces.

Now the fact that there is healthcare involvement in deciding the appropriateness of testing means that there are mitigations with that approach that will allow a lower amount of validations being done than for a situation such as being over the counter or OTC situations where there will unlikely to be healthcare involvement in selecting who buys the test and who performs the test and in what situations it's run. So we will be asking for a higher level of validation in that situation because there are not mitigations of a healthcare provider or worker being involved at all in the testing.

So those exact numbers are being finalized now. And so it would be premature for me to talk about that in detail. But when there is a prescription involved we're looking for the very least burdensome approach to this and it probably will be very similar to what we require, say, for a point of care test except in this case we're going to be asking that consumers, that people in the setting where you wish the test to get deployed are performing the tests, a minimal number of users in the usability study. And so they can demonstrate that they can get an accurate result.

So hopefully that's helpful. I'm hopeful that the home collection template will be out soon. And we are working on one for serology which will not be as

soon forthcoming.

Coordinator: And our next question is from (Cynthia Flynn). You may go ahead.

(Cynthia Flynn): Hi. Thanks for taking the call. I'm wondering for - if we're using an EUA kit from a manufacturer and we want to validate a different sample type, say, like we can use anterior nares or MT or OP or whatever and we want to validate saliva is it appropriate to just use the 30 positive, 30 negative and we could do that? Or because it's not our own EUA is that not appropriate.

Timothy Stenzel: As Toby mentioned earlier to me when I asked something that for this kind of change a bridging study is not the appropriate way to go. But we would look to the template recommendations. And...

(Cynthia Flynn): Right. Also the CT values. Yes.

Timothy Stenzel: Yes. So, that 30 and 30 is - if I remember correctly - is what we would recommend. The only thing that's different is of course if you're making a claim for an asymptomatic population. And then look to our recommendations on the EUA authorization required for that. And of course this doesn't apply to home collection and home testing.

Toby anything to add about that?

Toby Lowe: Yes. The only thing that I'd add this came up recently as an issue that we're looking as rapidly as possible to resolve is that there are actually no saliva collection devices that are authorized for this purpose. So we are working with collection device manufacturers to try to resolve that as quickly as possible to have more options be available for tests such as yours and labs such as yours where you would like to add saliva as a specimen type through the

modifications policy.

So we would encourage you to keep an eye on that. And if you have further questions about validation of saliva or about appropriate collection devices to use please reach out to us through the mailbox.

Coordinator: Thank you. Before we go to the next caller as a reminder if you would like to ask a question please unmute your phone, press Star 1 and clearly record your first and last name only so I may introduce you. We will be taking one question per caller.

Our next question is from (David Houg). Your line is open.

(David Houg): Thank you. First of all thank you guys for the ongoing interface. The transparency is really a model for how governments and industries should be acting. We really appreciate your incredible hard work. You know the situation among serology. We are in a situation with serology where if someone gets an EUA that the letter's published, no one can read it. If you look at an umbrella test the results of the validation in the umbrella test are shown. However there's no way to access validation for tests with an EUA which are not - did not go through the umbrella process.

There's no showing at all for the letter that was submitted on notifications. And nothing on notification validation result. What's the thought process then on why we couldn't have a notification - if people under the notification policy can offer their tests publicly, couldn't it be required that the letter that they submit and the validations results that they submit to get that notification would also be published so at least people who are using the test could read that information and decide whether it was appropriate or not to use that test?

Timothy Stenzel: So I think I want to make sure that I understand your question. I think what you're saying probably kudos that we're publishing some data, the NCI data as soon as we make regulatory decisions. And that transparency's appreciated. And of course any other assays that we authorize all the information that we receive in review and make the regulatory decisions on, on that are important to put into the instructions for use are there for the labs to view.

I think what you're saying is what are we doing for those tests that - and probably particularly for the serology tests - that notify us and have 10 business days to submit an EUA package? What information can be provided about those tests? Is that what you're asking?

(David Houg): About those tests but whether or not they're still in the 10 days or they've already submitted the EUA application. If they're out distributing their test in the market it should be just as easy for a consumer to look on the FDA Web site and see what the validation information they claim and the procedure for the test they claim and the notification as it is if an EUA is authorized. If the test is being consumed the information that a consumer can get on the test should be the same. That's the suggestion.

Timothy Stenzel: So the guidance - the current guidance is that through the notification pathway for the serology tests that developers can validate, notify us and then submit their data within 10 business days for our review. We do a triage when it comes in, make sure that there are no issues of public health importance. And then if there's no issue then they go into the queue.

Toby you can probably make sure that I'm correct in my response here. But we do require full disclosure by the developer of their performance. And that they follow the guidance and make the statement that we have asked them to do, that have limitations on this test. One is until authorized it can only be

used in a high complexity lab and all the other caveats that we've asked them to put.

Toby I believe we also - and before we post them - and this is what I want to verify with Toby right now. That we do verify that they have posted their performance on their Web site and only Toby noticed that can we - do we not prepare a notification up on our Web site? So Toby if you could confirm or deny that update.

Toby Lowe: So I am not positive if we do that for the notifications. We can look into that. But Tim's description of the process absolutely is spot on and we don't necessarily receive that validation at the time that they go on the notification list because they do have those 10 days before they need to submit it. And so we do - we do want the manufacturers to include that performance information on their own Web sites. But we cannot put it on our Web site until we have completed a review. And then we provide that information with an authorization.

Timothy Stenzel: That's correct. So we'll take the question of our process back. But we do require that they post on their performance and their instructions for use on their Web site. And if you know of somebody that isn't doing that and isn't showing performance even though they're notified then we would like to hear about it through our templates email or even at our FAQ EUA Web site or through the fraud line on that same Web site. Thank you.

Coordinator: And our next question is from (Piero Holitecio). You may ask your question.

(Piero Holitecio): Thank you for the acceptance of this call. Can you hear me?

Timothy Stenzel: Yes. We can.

(Piero Holitecio): Okay. Thank you. Yes. I have submitted a notification for EUA. And I also submitted a notification for a pre-EUA. But somehow I have been lost in the shuffle in that I've been assigned to several different reviewers and I have not been able to get a response from my reviewers. So I'm going to resend the letter out to the template email address to request another reviewer.

And I wanted to make this call last week. But I was unfortunately called on an emergency to do this. I would like just to have some attention brought to a high throughput serological test that I've been trying to develop but yet I haven't had the proper guidance I don't feel. And I've been working on this since February. So I'm frustrated as to why I have had several different reviewers and no follow-up. And it's a problem that perhaps others have had.

And I appreciate the question from the caller - the gentleman prior to us, two prior to us - that the notifications haven't been made public. So the people who would like to take them in our tests would - they don't see it publicly stated then they don't want to - they don't even want to bother with our tests. So something I think would benefit the entire population if something was made public that we do have notification in even though that we would state the directions on our Web site and that this would meet a proper usage by a professional and all of the bullet points that are required in our instructions which has been in all of my notifications.

And yet somehow I've been told that it's incomplete. I just want the guidance for the proper notifications then. Can that be had by me making this email to Toby or to Tim? Is that possible, sir?

Timothy Stenzel: Yes. So I've been making myself available to address some of these issues. So if you don't have my email address, which I'm not going to give over again,

then I might not be able to...

((Crosstalk))

(Piero Holitecio): I do not have your email address, Tim. I would appreciate it. If someone could forward me that email address directly. Because I need a reviewer that will help a micro company work through this process. I'm not (unintelligible). I'm not BD and so forth. Understand? So people that do some very interesting developments are really small companies and we need the guidance. And so we need someone who is adept at giving guidance. And unfortunately the people that have been assigned to me - and I know they're busy. But I would love to have some guidance and directed to someone who could give me proper guidance.

I would appreciate it. Because I feel like I have submitted proper notification, proper documentation, proper validation. And yet I have been refused and not got on the queue to be registered. And I need registration. Otherwise we're dead in the water. And I am sure that there are many people listening to this...

Timothy Stenzel: Hello?

Coordinator: And we go to our next caller (Dylan Beauchert). Your line is open.

(Dylan Beauchert): Hi. This is (Dylan) speaking. Thank you guys for taking the time to answer all of our questions. Mine is a little brief. But I was wondering when you guys will update prevalence for PPV and NTV calculations. I've noticed that LA County many others have shown much higher rates than 5%. The current estimate used by the FDA seems to give an appearance of lower validity for certain tests. And this will ward off certain healthcare providers who see these lower values although it might not accurately reflect the test

predicted values.

Timothy Stenzel: Yes. So the prevalence of disease and adaptive immune response can vary widely across the US right now. It's a good heads up for us to take a look at that from time to time and make sure that it is an appropriate prevalence for the vast majority of the US. As an example - it's only offered as an example and it is not meant to apply to each and every situation.

So we do - on that same Web site - we do provide a calculator to be able to plug in the actual performance and prevalence. And from the information even that is provided on our Web site insert the performance codes and the user or the end-user can see what the predicted positive and negative values are. So that tool is provided to all so that this can information can be made available to all and to look at the individual situation and make it specific for that situation.

So please feel free to use that calculator and encourage the folks that you're talking to, to use that calculator. And so we will take that back as to whether that 5% is still a good number to use on our Web site. We're unfortunately not going to be able to get every possible prevalence and not just high prevalence areas or low prevalence areas because it does matter what the prevalence is as far as the NPV and PPV.

(Dylan Beauchert): So thank you guys for taking the time and considering the - taking another look at that. Appreciate you guys answering all these questions and just working hard.

Toby Lowe: Quickly before the next caller I just want to follow up briefly on the previous caller if I could just have a minute to do that for the gentleman who was asking about his specific submissions. Apologies that you were cut off and

please do send an email and we'll follow up with you. I do want to clarify for everyone that there are very distinct pathways and if you submit a pre-EUA or an EUA that is not considered a notification.

If you are looking to be included on the notification list and to offer your test under that policy please be sure that you follow the instructions in that guidance to send a specific notification email to the EUA mailbox so that we are clear that that is what you are requesting and that that is separate from the pre-EUA or your EUA submission. That will help quite a bit with the process on our end and making sure that you get into the right place.

So again please send us an email so that we can follow up with you and we will hopefully get that resolved for you. Thanks.

Timothy Stenzel: Yes. And yes. My apologies as well. I was attempting to make some reassurances. But I am willing to get involved and provide some assistance in the situation. And I'm willing to do that for all companies who are in need of that. We have very busy reviewers. And when situations come up like this I do take them seriously. And I do look into them. So please send me an email to the template email address and ask for me, Tim Stenzel. And I will do my best to assist.

Coordinator: And our next caller is (Cody Luby). Your line is open.

(Cody Luby): Good afternoon, can you hear me?

Coordinator: Yes, thank you.

(Cody Luby): Yes, thank you for taking my call. Thank you for all the information that is given in this Town Hall. I have seen the recent last week on June 26 update

the FDA combating COVID-19 with their medical devices summary of all the tests that are given. It is well-intended and it is really useful for many, but at the same time, sorry to use the word it looks like discriminating. Yes, especially for those serology test developers who have notified FDA and whose names are there in the list.

As of today 193 manufacturers are there in the notification list. Of which I think around 11 are authorized. And about 182 are not authorized but in the notification list. But those names are not there in your recent June 26 announcement. And not only that, I think in general, word is kind of a considered like that but you have US stock regulations are involved, something like June 12th afterward if any developer has got authorization, their names are bold.

So, all these things will cause confusion. Already we are not able to sell our kit. Because many of the people are telling that you don't have authorization. And even though we say that the list is there a notification list, our name is there. And FDA in the Town Hall, time and again, mentioned that is good enough for people to buy the test and using the labs in the manner in which it needs to be used. But we are really having a very hard time in convincing those people. But this list stuff, giving the people that authorize and then you know, bold, putting the names bold in some cases, really are hurting us very badly.

Can you really do something to rectify and then help us, so that you know we can tell that our kits can be used in the lab? Really, we need your help.

Man 1: Toby do you want to take a crack at this, Or do you want me to?

Toby Lowe: Sure, we have a quick question for you. You mentioned that some are noted in

bold.

(Cody Luby): Yes.

Toby Lowe: Where on the website are you seeing that?

(Cody Luby): This is, I can send you the website, but it is actually the updated on 26 it is a complete list of FDA combating COVID-19 with medical devices. So, in every page on US authorizations are in bold. So, it kind of gives all the authorizations not only in vitro diagnostics and medical devices and everything. And some other kits are the manufacturers are their names are bold, because authorizations (unintelligible).

Toby Lowe: Right. So just to clarify on that document. The bold is to indicate what has changed from the previous version. So, every time that document is updated the new additions are included in bold. I don't think that we had intended for the bolds to be interpreted as anything other than an update. So, I will provide that feedback to the people who maintain that document. On our on the IVD specific authorization page, the new authorizations are simply added to the table. So, they're not, you know, they're not indicated any differently, other than to include the date they are added to the table. And then, the notified tests are listed separately on the notification list on the FAQ page.

So, there's not really any way for us to note them differently because they are being offered under different pathways and we have not reviewed them and authorized them at that point. As soon as we do authorize them, they, as you mentioned, are noted as authorized and they are included on the EUA list.

(Cody Luby): What I'm bringing to your attention is the problems that is there in the real world. When we say our test is in the notified lists and we show our

instructions for use, we show the performance. It is as good or better than the authorized test. But the customers are specifically asking to show us the authorization letter, then only we can buy. So, that is not the thing that you have been telling in the Town Hall, but that is the notion that is there in the customer.

So, can you do something to tell them that's not the case?

Toby Lowe: I can take that feedback, and see, you know, think about what might be able to be done.

Timothy Stenzel: Yes, I would just say that we're open to those things, but it's not clear to us what more we can do than we already tried to do on this Town Hall and website. Thank you for your call. I do want to make sure that we get time for additional problems.

Coordinator: Our next question is from (Elko Wershocky). You may go ahead.

(Elko Wershocky): Thank you. I had a question regarding the criteria for controls in the EUA kit. And that's for the CT values, and it's for the positive controls and also the internal controls. And for quite a few of the kits. And it's not unique to coronavirus, it's also involves other FDA approved assays the CT values for acceptable criteria are often less than 40. And that results in a very wide range of acceptability. So, for example from 10 to 39. And I'm just wondering why the criteria for CT accessibility isn't much tighter, like 28 to 34. And also having tighter criteria for the internal controls allows for better assessment of inhibition in individual patient samples. So that's my question. Hopefully, it's clear.

Timothy Stenzel: Yes I think what you're asking is how can we better control with an internal

control the assay for our SARS-CoV-2 and for adequacy of collection and for the adequacy of the extraction in the population of the sample. I think your question is and how we can tighten up those specs. Is that the question.

(Elko Wershocky): Yes, for both the internal control and then also like the positive controls in the kit. The CT range is often like less than 40. That can result in huge variability and it makes it more difficult to assess issues, you know instrument or extraction problems.

Timothy Stenzel: Yes. I understand and where developers have months or years to develop a test and optimize all of these things. Those are obviously things we would hope to see. And, however, in responding to an emergency situation and are interest is to provide as much testing that we can determine is as accurate as possible and as quickly as possible. You know, that's their mission as of right now. These are excellent points as some of these tests start converting into regular authorization, developers should consider this. Because this is an important element that you would like to see in all tests, that we have for more routine not emergency authorization.

You know, I think those developers are sometimes doing that during this emergency and show that in their development and in there data may have, you know, adapt over others that don't do that. So, point very well taken. Ideally we would actually love that. And as we move forward in this pandemic, we have updated the requirements for validation doing some contrived samples and actual samples. We've been updating some of the assays with postmarket requirements.

So, it is an evolving process and it's a good point to make and we will take it back to the team to assess how we might incorporate that thinking into the future test developments. Thank you.

Operators: And our next question is from (Thomas Wilchard). You may go ahead.

(Thomas Wilchard): Great. Thank you for taking my call. I want to make a couple of brief comments. I apologize, but they're going to frame the context for my question. Look, I think we all can agree that we are entering and going to experience a massive increase in the rate of infection. We need to come together and do a much better job of working together as an agency and an industry. In particular, regarding the distribution of kits. My question is regarding, or what I will call serology in a general tests and also, in particular, the currently in limited supply production antigen test, okay.

I'm wondering why we don't all take a more robust view of what I'll call lateral flow pinprick antibody test. And these new (unintelligible) swab antigen tests as a triage system, a first line. If we are going to increase testing capacity at the rate that we need to, we have to turn and make it much easier for distribution of both of these types of tests, because we're not going to have the capacity, as we learn from Quests when they release a press release a couple of days ago, talking about limited supplies and problems in the near future for virus microbiology test.

So, my questions are these. Number one, for these types of triage devices where everybody understands that you get this test, it's not as accurate, you have to have it followed up. Why are we not seeing a more robust system and in larger numbers of these tests being allowed to be distributed through a CLIA-waived designation? It seems like these tests are not that complicated. People that have a waived CLIA designation have plenty of experience. You don't need to have - to the extent that we are continuing to limit, a pre-EUA to highly complex CLIA lab. These antibody tests and similarly these antigen tests as well. And only after EUA expanding them to moderately complex.

The difference between the ability to distribute these tests. Three designations for the CLIA lab is massive. Okay. If you could move to a system where you allow these types of triage first-line tests that are widely available, cheap to make and can actually be brought out to the public to be done on a waived basis. Okay. That is going to solve our problem as an industry and yours as an agency of getting robust testing out to the public.

Currently, I understand your position, you intend to be more

Timothy Stenzel: Maybe you can be a little more direct in your question.

(Thomas Wilchard): How about this, why do we need to, why does every person who has gotten an EUA for example for an antibody test, and received an EUA for a highly complex and moderate complex have to go back and go through the long queue right now of an amendment to the EUA to expand that to a waived CLIA designation. When we know exactly how these tests operate. We know what personnel are able to do them. It doesn't make any sense.

Timothy Stenzel: So, we've authorized tests, one antigen and four molecular tests for the CLIA waived environment. And we're very interested in authorizing more. And we've provided validation details in our serology template, as well as in our antigen template. And so, once those studies are performed I have directed our office to make point of care testing a priority.

So, you know, as soon as there is point of care data to review on an application, whether it's an original or an amendment. It is a high priority and if somebody has a point of care test with all of the point of care studies in it all ready and it has been submitted into our office and they're not undergoing

interactive review within a few days of submission; I would like to hear about it. You can send an email address and ask for Tim. I'll look into what the issue is. But high level direction to the office is when we have point of care test data to review that is priority.

Now, something may have been designed for a point of care setting. But, if we haven't had data showing that it can perform accurately in that setting, we are unable to authorize that. And so, we have provided detail, and recommendations on validation to get that deemed CLIA waived. And we can provide that for the molecular point of care now informally and we are working to update the template for the molecular template to allow the point of care recommendations for validation to be there as well.

Coordinator: And our next question is from (Andrew Louaday). You may go ahead. Andrew? He dropped out of the queue.

Our next one is from (Ray Bandovo). You may go ahead. And again, (Ray Bandovo), your line is open. We are not able to hear you.

And our next question is from (Gretchen Johns). You may go ahead.

(Gretchen Johns): Hi, this is (Gretchen Johns) can you hear me?

Timothy Stenzel: Yes.

(Gretchen Johns): We're having a lot of trouble getting reagents, which I know everyone is just before our high throughput instruments and rapid tests. I was wondering what's the status of pooling and are there any vendor-approved EUAs for pooling or do you have to do that on your own or, you know, it's getting to the point of desperation. So, any help you can give us that that'd be great.

Timothy Stenzel: So, we are absolutely open to pooling. We have not authorized a pooling scheme yet. We are asking for EUA submissions. Labs or manufacturers can come up with their scheme, validate it and notify us and submit within 15 business days. And we'll review those schemes and look to authorize them. You can use, for this, you can either use your own EUA authorized test or you can use a manufacturers' test to do this. And, we've started looking at some preliminary data about pooling. It's not unfortunately going to be a panacea. Yes, it will address reagent shortages. Yes, it can expand our capacity to test more and more patients with the given infrastructure that we have, but nearly all pooling schemes will reduce the sensitivity of the assay. And therefore, we do predict that patients, especially low positive patients may be missed in pooling schemes and called falsely negative so we've made the recommendation that negatives are called presumed negative when samples are pooled, just to alert the ordering clinicians or healthcare workers that if clinical signs and symptoms warrant, they may want to follow up with a non-pooled test for certain patients. And the other thing is early preliminary data suggests smaller pools are more likely to have less sensitivity drop, which makes complete sense.

So, we would urge caution in this approach and fully validate your pooling scheme. And have a pretty robust design, so that you know that if you're missing any positives that it's a really low amount. But given the situation, we understand, and we'll be working with developers, we're updating information about pooling, pooling schemes. And some of the concerns we have and some additional guidance once we gain more information about which pooling scheme may be working the best and minimize the test with false negatives. But some of the early data that we've seen, suggests that there could be a larger percentage of false negatives, depending on the population that you're pooling. So caution is warranted here.

Let's see, what other things could come up. The important thing is that one of the pooling schemes that may have less risk, although not zero for false negative is to put multiple swabs into one VTM. You could have potentially increased inhibition that needs to be guarded against. Obviously the other challenge of doing that is, how do you de-convolute a positive pool and know which one of the swabs was positive. So, the schemes for that are unfortunately complicated as well because they either mean going back to everybody who is in that pool or requiring two swabs of each individual and then swabs are often in short supply.

So, this is a very challenging situation. The FDA is open to it. We're out of an abundance of caution, we're asking for submissions and EUA authorization at least for the time being so we can figure out which schemes are going to work. We are, and we are encouraging all manufacturers to come in with pooling applications as well. So that those are automatically, you know, once they are reviewed authorized available for customers to use.

Coordinator: And our last question is (Nate Masely). You may go ahead.

(Nate Masely): Hi. Can you hear me?

Coordinator: Yes, we can.

(Nate Masely): Hey, actually my question I'm a pharmacist and I think you just answered my question. It's regarding the pooling testing, and we were looking at the potential strategies of how to do that. If you had a positive in the pool. And as we were considering is having each patient do two swabs so that once the pool came back positive, you'd have a second swab. It sounds like that's something you're considering, but there may be a shortage of swabs?

Timothy Stenzel: Yes. It does put pressure on swabs which have been in short supply at times, currently. And also, what do you do if you have a high volume, what do you do with those swabs, how do you store them, how do you inventory them, how do you go back to them easily. So, unfortunately, there's no, you know, ideal options here. I'm just saying that the FDA is open to different options and wanting to work with developers on what will work for them. And of course, it all depends on the incidence of positives in your population.

So, some pooling schemes, particularly combinatorial schemes, . they don't work, for really high prevalence, high incidence situation where the prevalence of positive results is high or the incidence of positive results is high. And the, you know, most of those are relatively low. The low incidence populations, low prevalence populations are going to be better for combinatorial schemes and simple pooling is going to be better for higher prevalence but once you reach about 20% positivity almost any pooling scheme is less ideal.

Coordinator: And that concludes today's question and answer circle, I like to turn the call back to Timothy Stenzel.

Irene Aihie: Hi (Lesley). Thank you. This is Irene Aihie, and 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 by Tuesday, July 7. If you have additional questions about today's presentation, please email cdrh-eua-templates@fda.hhs.gov - and 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: And this concludes today's conference. Thank you for participating. You may disconnect at this time.

[End of segment]