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

Moderator: Irene Aihie
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Coordinator: Welcome everyone to today's conference call. At this time your lines have been placed on listen only for today's conference, until the question-and-answer portion of our call, at which time you will be prompted to press star 1 on your touchtone phone. Please ensure that our line is unmuted and please record your name when prompted so that I may introduce you to ask your question. Our conference is also being recorded. And if you have any objections you may disconnect at this time. I will now turn the conference over to our host, Ms. Irene Aihie. Ma'am, you may proceed.

Irene Aihie: Thank you. Hello. I am Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 43rd 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 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 line for your questions related to the development and validation of tests for SARS-CoV-2. Please remember that during this town hall we are not able to respond to questions about specific submissions that might be under review. Now I give you Timothy.

Dr. Timothy Stenzel: Wow, 43 town halls to date. That's a lot. And we'll keep going as long as you all think this is helpful. And these sessions are designed to provide assistance to all COVID-19 test developers, whether they be molecular, antigen and/or serology tests. That's why we do this.

And obviously, we have a lot of interaction with essentially all developers who have submitted a question or an application to the FDA through our office. And those are happening sometimes 24/7. And that's how we do it. I wanted to give an update on authorizations.

As of yesterday evening we had authorized 331 tests and sample collection devices including 247 molecular tests and sample collection devices, 70 antibody tests and 14 antigen tests. There are 37 molecular authorizations that can be used for home collected samples. There's one molecular prescription at home test, one antigen prescription at home test, and one over the counter at home antigen test.

We expect to see more home collection kits come in, in wider availability through that, including when prescriptions are not required in that home collection kit we are calling it direct to consumer and you can search on the FDA authorized Web site for any direct to consumer home collection kits.

When it's a test in the home we're calling it over the counter and - when it's not prescription.

We expect more collection kits including more direct to consumer kits, and more at home tests including more OTC at home tests. So those are obviously priorities along with very high throughput central lab tests. So with those brief updates let's move right into questions. And we look forward to hopefully helping you out today. Thanks.

Coordinator: Thank you. At this time if you would like to ask a question, please press star 1 on your touchtone phone. Please ensure that your line is unmuted and please record your name when prompted so that I may introduce you to ask your question. Our first question is from Shannon. Your line is open.

Shannon Clark: Hello. Shannon Clark here with UserWise Consulting. When we conduct home use human factors testing it's inappropriate to ask laypeople or the participants, to please read and follow the instructions as users when using the product. And since typically participants refer to instructions less than 60% of the time, after they're finished using the product we typically ask user manual comprehension questions to assess the understandability of the instructions.

So for over the counter human factors testing for antigen tests and home use molecular tests, does the FDA require user manual comprehension testing or does the FDA acknowledge their own 2016 human factors guidance indicating that a sample size of 15 participants is adequate for uncovering usability problems with the instructions?

Dr. Timothy Stenzel: I don't believe we require the questionnaire at the end. Toby, do you known on that, or recommend it, rather? I don't believe that we recommend the questionnaire at the end. I think it's nice to have. It's nice to have if there

are any issues in the testing, so that you can drill down to if you, you know, if any updated instructions are going to be helpful for redoing the study with the modifications to make it work.

But I don't know that I - that that questionnaire afterwards is recommended. Toby, do you have that information today?

Toby Lowe: Right. I don't believe we currently have that as a recommendation in the template. We do think that it's important to consider usability and end user comprehension for - especially for over the counter tests when there would be no involvement of a healthcare provider and that is something that we consider is the appropriateness of the labeling for a lay user.

But we do not have a specific recommendation for that questionnaire in the templates right now.

Shannon Clark: Yes. I find that labeling defects tend to shine through during simulated use anyway. So asking questions after simulated use or actual use doesn't really add too much, but prolongs all the sessions and makes it more costly.

Toby Lowe: Thank you. That's…

Dr. Timothy Stenzel: Okay.

Shannon Clark: Thank you.

Coordinator: Thank you. The next question is from (Brian Jones). Your line is open.

(Brian Jones): Hi. Thanks, Tim. So I tried to ask this question last week and was cut off at the end of the call. This is just for some clarification about testing paired

saliva and NPS specimens. So the first part of my question is that the EUA template doesn't seem to have any information regarding the investigation of discordant results.

And I was wondering if you had any suggestions on how to do that, for example, testing on a separate EUA that was already authorized for use with NP, even if it wasn't already authorized for saliva, if that would be a sufficient investigation.

Dr. Timothy Stenzel: So the NP swab when validating oral fluid or saliva, that is a recommendation using NP swab. The NP swab we recommend you use a high sensitivity molecular assay with an extraction in the procedure, as the comparator. Now you could have discordant results between saliva and that NP result.

Hopefully minimal, but we've seen it in some cases and, you know, from early days. And for whatever reason, some saliva used in some assays, does - and oral fluids, does present a challenge for some assays. So that's why we continue our recommendation for NP swabs. So I think hopefully you're still on the line, you can clarify your question about how to resolve discordances between a comparator test done with the NP swab and the candidate test done with saliva.

(Brian Jones): Yes. So in this particular case the test that we are validating for saliva already has an EUA for NP. And I've seen that at least in some cases there have been EUAs, grant authorized for manufacturers where what they did is they compared their performance of their test on saliva and then also used their test as the performance for the comparator for NP swabs.

Dr. Timothy Stenzel: Yes, I think that…

(Brian Jones): Because it…

Dr. Timothy Stenzel: I think that's okay. So what you're saying is…

(Brian Jones): And so that would - that's what we would plan to do is to…

Dr. Timothy Stenzel: …one for discordance, what do you do with the discordant?

(Brian Jones): Right.

Dr. Timothy Stenzel: And what would be false negatives in saliva or false positives in saliva, or both?

(Brian Jones): Yes. Either way wherein both cases our test, the candidate for saliva our test is what is being used to test both the saliva and the NP specimens. So I'm proposing that we would use another EUA that was authorized for NP and we could test those specimens to try to do that discrepancy analysis.

Dr. Timothy Stenzel: So back to the original question, we may obviously prefer a different test be used as the NP comparator test than the one you've developed. It's a little bit cleaner that way as far as, you know, a good - it may be in earlier days we didn't have many options too, so we may have allowed them. On the other hand, if we've allowed it in the past and you want to pursue this route I would get, you know, I would get concurrence on the FDA review team through your interactions, you know, directly with the reviewer or through the Templates email address or a pre-EUA.

You can use a composite - you can do discrepant resolution. I forget what our minimum recommendations are. Probably if you want to, you know, resolve

both positives and negatives that you do equal numbers of both. The table could be annotated if you do that, which means in the footer you can explain what the alternative method results are.

It should be another high sensitivity comparator test with an extraction, molecular test. There is a way to do a composite result. So the comparator rather than being a single test could be two or more tests. If you do that for all samples you can have a composite comparator. There would need to be rules established like perhaps it's both tests could be positive or only one could be positive.

Again, if you're going to go that route, I would double check with our review team. Okay? Hopefully that's helpful. But it's certainly allowed to do resolution of those discrepants. But we would need a minimum number of data points to be able to display that in the footer.

(Brian Jones): Okay. Thank you.

Coordinator: Thank you. Our next question is from (Elaine Allen). Your line is open.

(Elaine Allen): Hi. Thank you very much. My question is in relation to the notification process. We followed the guidance in the information online in the Notifications for Emergency Use Authorizations FAQs for commercial manufacturers distributing serology test kits. Our assays validated. We notified FDA appropriately, of our intent to distribute and intent to submit our EUA accordingly.

It was our understanding that once we notified FDA and received notification via auto-reply that we could begin to distribute. However, FDA replied we could not begin to distribute until the notification was accepted. Would you

please update - provide an update on the notification acceptance process and timing? Does FDA ever deny distribution at this stage? Or is this a formality to be sure everything is in place?

Dr. Timothy Stenzel: So from the beginning you get an email response that says that you had submitted, you know, it's an automated response. But our team assesses the request and makes sure that some key boxes are checked there, to make sure that it's something that we can allow to go up on our notification list. So the official response for allowing notification comes in a subsequent email.

We typically try to turn that around pretty quickly. So if it is taking more than 48 hours and two business days to get a response, I would ping them again, and I would also - you can let Toby and I know, through the Templates email address and we can look into a specific situation. Hopefully that's helpful.

(Elaine Allen): Yes, that is very helpful. And I just want to say the response team has been wonderful and they're very quick. And I just wanted to place that out there. But we were just a little confused on when we could start to distribute. And so I'm assuming there's one final email that will come in that will say we're good to go?

Dr. Timothy Stenzel: Yes. You'll get an immediate response and then it goes to our review, our quick review team to make sure that the - everything's, you know, there for proper notification and place them on our notified list.

Toby Lowe: And just to…

(Elaine Allen): And then…

Toby Lowe: …add to that, because we have had…

(Elaine Allen): Oh…

Toby Lowe: …you know, some situations where developers have sent notifications for tests that are not eligible for the notification policy. And so just to clarify for everyone, obviously I don't know which test you're referring to so I don't know if this applies to you, but just to clarify, for everyone listening, you know, one of the areas especially for serology tests, is home collection with dry blood spots is not - and home collection at all, for both serology and diagnostic tests, is not eligible for the notification policy.

So that is one area where we've seen a number of notifications come in that we've had to respond back to the developer to tell them that they cannot distribute yet, because that is not under the notification policy.

(Elaine Allen): Oh, okay. Good. That doesn't apply to us, so I'm happy to hear that. Oh, I'm sorry, did I disconnect?

Toby Lowe: No. No.

Dr. Timothy Stenzel: You're still on.

Toby Lowe: You're still here.

(Elaine Allen): Oh. Oh, okay. I heard a strange - all right, so they did come back with some comments on what they'd like, to see in our IFU. We confirmed that we had made those changes and…

Dr. Timothy Stenzel: So, so…

(Elaine Allen): …I suspect…

Dr. Timothy Stenzel: You know, we don't really want to get into the specifics of any one application. So…

(Elaine Allen): No. I understand.

Dr. Timothy Stenzel: …we can answer general questions here or give you information on how to resolve anything with Toby and I, or with the review committee. But we don't want to really get into the details of…

(Elaine Allen): Yes. I understand. I'm sorry about that. Thank you very much for your time. I appreciate it.

Coordinator: Thank you. Our next question is from (Eli Railbot). Your line is open.

(Eli Railbot): Yes, hi. I was just wondering regarding getting the tests for the person to take at home, the home tests, I've heard different options that are going to be available either in CVS pharmacies or even that you can just pick up or get sent to your home and buy them on Amazon even. Is there any specific date that - because that will make a big difference for us to get our kits back out and to go back to the public so to speak, if we can take these home tests, so we know where we're standing at least 90% if it's accurate?

Is there a specific date that we know that those are going to be available for just the regular people to be able to pick up at CVS? And if there will is there a specific brand that we know we have to look for? Thanks.

Dr. Timothy Stenzel: Yes. So, you know, the FDA does not develop tests. We review test submissions and look at to make sure that it's an accurate test, and if we can

authorize it, we'll authorize it. We also don't - can't really tell a developer how they go ahead and commercialize. So once we've authorized an at home test or a home collection kit that goes up on our Web site and it's really, you know, up to the test developer to figure out how they make that available to patients and consumers.

In some cases the US government funds efforts to make these tests widely available and you've probably seen some press announcements about that. So again, it's not up to the FDA how these - what a given manufacturer does once they get an authorization, as long as they're promoting it appropriately for what we authorized.

(Eli Railbot): Got it. I appreciate that. Is there any on the horizon that on your part is approved, and then up to them how to market it?

Dr. Timothy Stenzel: Oh, all of them are that way. And we've authorized three at home tests. One is over the counter and two are by prescription. And then we've authorized what did I say in the beginning, over 30 or 40 home collection kits. Some of those home collection kits are available direct to consumer already. Again, you can look at the FDA Web site to see which ones those are.

And reach out to the companies and they will inform you about how you can get a hold of their test or…

(Eli Railbot): Thank you. Okay. I appreciate it. Thanks.

Coordinator: Thank you. Our next question is from (Kodomuti Venkat). Your line is open.

(Kodomuti Venkat): Good afternoon. Thank you for taking my call. Many times, you know, it is mentioned that in terms of priority of reviewing, especially the serology test has a low priority and the high priorities are the home collection kit and the

antigen test and the (unintelligible). And one of the thing the high priority, the high throughput test can FDA give a description or a definition what is considered high throughput instead of making some subjective determination?

Is there any - a little bit more insight into what constitutes a high throughput test please?

Dr. Timothy Stenzel: So yes, high throughput is something that can be fluid. And so we haven't posted that information. But you can check through the pre-EUA process or perhaps send a question to the Templates email box if your test would qualify as high throughput.

And as far as the other priorities, serology tests that are point of care; serology tests that are at home; or serology collection - home collection kits; as well as serology high throughput tests, are all high priority tests. I would also say that neutralization tests, serology neutralization tests are also currently high priority. We've only authorized one.

And so when we get any subsequent neutralization assay submissions we make them all high priority right now. Yes. Hopefully that clarifies it. Serology tests in those categories are high priority. Thanks.

(Kodomuti Venkat): The serology tests for vaccine differentiation, vaccination whether the infection, is it a priority or previously you mentioned that it has to go through CBER. Can you give a little bit additional information please?

Dr. Timothy Stenzel: Yes. We haven't authorized any tests there. But we would work in conjunction with CBER. And if someone comes in with a complete clinical trial showing, you know, basically efficacy for a test that predicts vaccine either someone needs vaccine or someone who's benefited from the vaccine,

they come in with complete data for that, we would try to move that along pretty quickly as well.

You know, it's a pretty big ask to show that we can use test information in that way, other than, you know, you've developed antibodies or not, which is an easier validation.

(Kodomuti Venkat): Thank you so much.

Coordinator: Thank you. Our next question is from (Kristen Bankert). Your line is open.

(Kristen Bankert): Hi, yes. Thank you for taking my question and hosting these town halls. At last week's town hall a caller had mentioned - it was - they were advised during the pre-EUA review that it would be acceptable to use an EUA authorized multi-analyte test for the detection of flu targets this year. However, beyond this year it would require a de novo or a 510(k).

Do you have any updated thinking on this topic, specifically will this be required for all multi-analyte tests, as we did not receive this feedback during EUA review? And for the clinical studies needed to support the de novo or 510(k) conversion, will it be acceptable to use flu retrospective specimens since flu prevalence is low this year?

Dr. Timothy Stenzel: Yes. No. Thanks for bringing that question up. Actually we had - we forgot to announce that at the beginning of the call. So I think there was some confusion, you know, that there was some confusion with a particular reviewer on that topic, but we've clarified that.

So the bottom line is that I think the topic had spun to what would happen if the emergency declaration ended, rather than, you know, if something is EUA

authorized how long can it be on the market? And as long as there's an emergency. I anticipate this emergency lasting years and we have prior emergencies that have not been undeclared.

You know, EBOLA and Zika and Enterovirus perhaps among others, are still open emergencies even though we're years past them. I expect that to be the case for COVID. And in which case there will be no rush by anybody to at least from the FDA, to convert these.

Now we are developing a guidance that will guide developers who want to convert and should an emergency no longer be declared, we'll provide for we hope a reasonable timeline for developers to convert their assays from an EUA to a full authorization.

So, you know, bottom line is I believe there was a misunderstanding and a panel test that's authorized via an EUA will in all likelihood, be able to stay on the market given no problems, for as long as the emergency is declared and can be used not just this season but next season as well. So hopefully that clarifies that.

(Kristen Bankert): Yes. Thank you very much.

Coordinator: Thank you. Our next question is from (Lisa Neibauer). Your line is open, ma'am.

(Lisa Neibauer): Yes, hi. Thank you very much for taking this call. I just had a question regarding how FDA is viewing the recent studies that compare PCR to culture and specifically, show that for CT values over 30 those are really considered a noninfectious sample. So as it pertains to the comparison for antigen PCR is

it really relevant to have that comparison in populations with a CT over 30 given these studies?

Dr. Timothy Stenzel: It is important. That's a question that we get frequently. The CDC, APHL, and CAP have all said that CTs cannot be used to determine infectivity. Culture is a notoriously insensitive method. Now if you're positive via a culture method then you would know there was intact virus that would potentially infect others. But a negative doesn't mean - well I have not seen any outcome studies relative to this hypothesis and I think it may not be ethical to put people at risk of contracting the virus just to test a hypothesis like this.

I think if you searched the literature you will also see that - and we have data that's not public, that in the first five days of symptoms patients can have very high CTs on any given molecular result, a comparative result. As high as 40 and but well over 30. In fact, we often see up to 25% of the results from the first five days of symptoms, above 30.

You know, someone who has symptoms in the first five days of symptoms and then has COVID confirmed by a high specificity, high sensitivity molecular assay, probably needs to be deemed potentially contagious. So that's, you know, that's just science. And, you know, that's what we're basing our decisions on.

Now that said, we are encouraging all rapid to come in. Rapid tests can get authorized, you know, we've authorized tests that have only been examined in the first five days of symptoms. And, you know, if they perform well in those first five days when people were generally thought to be more infectious, compared to molecular tests, which is comparisons made there for accuracy.

We want to know if patients in the first five days of symptoms, really have COVID or not. And, you know, molecular is the gold standard to tell us that.

We are not looking at whether an antigen test is accurate, you know, two weeks out or three weeks out. So we believe this is a very reasonable recommendation for validation. The other thing is that, you know, we just don't know for sure although I think there's some data that's creeping out. You know, what the initial - when someone first begins to shed virus, you know, is it really high amounts or could it be really low amounts?

And we look forward to seeing what that portends. But we would love to see a direct diagnostic test perform very well in those early days of viral shedding. So hopefully that addresses the question. It may not be what you want to hear, but…

(Lisa Neibauer): Yes. Thank you. I think the only thing I would add is just that we have seen on the NIH Web site that there is really not a correlation between CT value and days since symptom onset. So I think it's a little difficult to use days since symptom onset as some sort of a marker. Perhaps consumers can't recall or don't know that number very accurately. So, thank you.

Dr. Timothy Stenzel: That's - yes, no, I see. But there is- the other thing to say about CTs in APHL, American Public Health Labs, CDC and CAP, College of American Pathologists, have stated very clearly that you cannot compare CTs between assays even within the same assay and the same lab between different technologists; down to that level.

The molecular assays that we've authorized, none of them are quantitative. They have not been validated to our knowledge, at least not the ones we've reviewed. They haven't authorized a quantitative molecular assay or semi-

quantitative molecular assay, which would require at least two point calibration and demonstrating good linearity over the dynamic range of the assay.

And at least two lots of calibrators and probably three lots of reagents, because there can be lot to lot variability. We want to know that the calibration can be set across lots and be consistent so that you get accurate, quantitative, semi- quantitative data over time with an assay. So we - again, we have not authorized a single one of those.

I'm not seeing a lot of interest in that, but if you want to be truly quantitative that's the way to go. The challenge with that is even if you have a quantitative molecular assay, a very good molecular assay, it's pretty clear to me at least, and I think many people, that a respiratory sample from a swab, you know, is just not something that is going to be consistent throughout a day or over time. There are other variables when you're doing sampling in the nose or perhaps even sampling saliva in the mouth.

You just can't count on consistent virus shedding through a day or over days when somebody is infected. It's different from other true quantitative molecular assays for example, for - which are blood based, you know, for say HIV, HPV, HCV. I mean those are excellent assays that have been authorized by the FDA and all of the sample type, whole blood often, that is well-mixed and is a reliable sample type for determining viral loads and monitoring patients, particularly HIV and HCV patients through therapy.

So longwinded answer there but we get this so often I wanted to be a little bit more complete about our thinking on this topic. Thanks.

(Lisa Neibauer): Thank you. Thank you very much.

Coordinator: Thank you. Our next question is from (Anne Wright). Your line is open, ma'am.

(Anne Wright): Hello. Thank you for taking my question. I have a two part question. One is - the first one is in regards to the EUA guidance for antigens. Is the expectation that, you know, once we get the authorization expectation is before release and distribution, are we supposed to complete our design control portion first, prior to, you know, being able to distribute it?

Dr. Timothy Stenzel: Yes. We waive most design control requirements in a - with an EUA authorization. That's pretty standard.

(Anne Wright): Okay.

Dr. Timothy Stenzel: We've done that for all of the assays. We require a couple of things. We require you to do MDR reporting and complaint handling.

(Anne Wright): Okay. Okay. After distribution.

Dr. Timothy Stenzel: Toby, is there anything else that we require as far as design controls and quality system requirements?

Toby Lowe: I believe that's it. The best way to check would be to look at a recent letter of authorization for a test that is similar to yours, and look at what we have waived versus what we've required.

(Anne Wright): Okay. Okay. All right. We'll do that. And the - oh, sorry?

Dr. Timothy Stenzel: You had a second part, you said?

(Anne Wright): Oh, yes. Yes. Yes. So - oh, just continue on the first part to make it clear. So if you are kind of basically using it that you want to potentially use the data for later on for the 510(k) submission for the future, is it advisable I guess, to basically, you know, create your DHS and make sure that you have all your data ready so that you could, you know, be prepared for the future 510(k)? Would that be advisable?

Dr. Timothy Stenzel: Yes. That's an important question, and we've certainly seen a lot of new developers, new at least to the FDA. We may not have FDA compliant quality systems in play in the guidance that I mentioned earlier on this call, the transition from EUA to full authorizations. We'll address the quality system requirements as well during that transition. So if you know you want to transition to a full authorization, you know, it doesn't hurt to start working on that now and get…

(Anne Wright): Okay.

Dr. Timothy Stenzel: …something in place. But look to the…

(Anne Wright): Okay.

Dr. Timothy Stenzel: …guidance once it's made available for more details on that.

(Anne Wright): Okay. But it's not available yet?

Dr. Timothy Stenzel: No.

(Anne Wright): Right. Okay.

Dr. Timothy Stenzel: And Toby, you had something else?

Toby Lowe: Yes. I just wanted to clarify. I believe that there are three portions of 820 that we do not waive. Those would be acceptance activities, nonconforming product and statistical techniques. So you can take those…

(Anne Wright): Oh, statistics? Okay. Okay.

Toby Lowe: …you can look in one of the recent authorizations as well.

(Anne Wright): Okay.

Toby Lowe: And also, you know, to what you were asking about, you know, preparing for a 510(k) or future use, you know, we also don't object to do any, you know, tests that's under EUA being developed under a full compliance quality system. That's preferable. But we do waive certain aspects of it.

(Anne Wright): Okay. So basically continue on with post-market activities?

Toby Lowe: Right.

(Anne Wright): As is at the time of release. Okay. All right, thank you. And my next question is under the stability test guidance document it's not clear to me whether the expectation is to also include a test for operating conditions, basically like at room temperature, how the device will, you know, the reagents will like operate and make sure that they're, you know, still operating as intended.

Dr. Timothy Stenzel: If it's a point of care test or it's a home test.

(Anne Wright): Or near. Yes.

Dr. Timothy Stenzel: Look to the flex studies.

(Anne Wright): Okay.

Dr. Timothy Stenzel: And look to the variables that may impact your test performance. Temperature can be - very well do that, but again you can do that with bench testing. You don't have to do that in the field in a home, or in a home…

(Anne Wright): Correct. Correct.

Dr. Timothy Stenzel: …situation. Or in a clinic. Okay?

(Anne Wright): Okay. But you should…

Dr. Timothy Stenzel: But the other thing I should add about quality systems and regulations, there are some times when we'll add into the letter of authorization some additional quality system requirements that we don't standardly ask for all - necessarily for all EUA authorizations. So there may be some specifics that may be technology based or may be specific for a particular test, that came up during our review.

So again, I think Toby's recommendations are great. Look at some recent authorizations that…

(Anne Wright): Okay.

Dr. Timothy Stenzel: …mimic what you're doing for that. And then obviously, ask the reviewer when you submit.

(Anne Wright): Okay. So your patient test and point of care testing would be kind of considered equivalent in terms of that, right, in terms of the operating conditions evaluation?

Dr. Timothy Stenzel: Yes. Yes. Yes. Look at our templates for whatever technology you have for the point of care. And it'll have the - a list of sort of like suggestions, recommended flex studies. But each developer decides which one apply generally to them. But you can also look at recent authorizations at the instructions for use and those kinds of flex studies I believe should be described. They may not be - may not show all our results but they may be described in written form for the ones that we…

(Anne Wright): Okay.

Dr. Timothy Stenzel: …have authorized. And that'd be a good indication of what - if you look at a similar technology to yours would be asking for flex studies.

(Anne Wright): Okay. Thank you so much.

Coordinator: Thank you. Our next question is from (Luis Jimenez). Your line is open, sir.

(Luis Jimenez): Hello. Thank you for having this meeting. I just wanted to ask in terms of the point of care validation, is the FDA accepting the information - the validation information from outside the US or is it a requirement to do a clinical trial in the US, for example, would Canadian data be acceptable?

Dr. Timothy Stenzel: So we do recommend that point of care studies and home studies are done in the US. It's sometimes very challenging to assess how closely settings outside the US would mimic settings inside the US. And we've clearly seen

some developers do "point of care" study in, you know, central labs with trained - fully trained laboratoriansAnd that’s obviously not.

And that may be where point of care testing is done in some countries. But it's not where it's done in our country. So that is our recommendation. If you want to do something different I would submit a pre-EUA and outline what you would like to do and see if it's acceptable to our review team.

(Luis Jimenez): And the point of having some type of bridging study, do you have any general recommendations to be able to leverage existing data to merge it with US centers?

Dr. Timothy Stenzel: Are you talking about point of care studies?

(Luis Jimenez): Yes.

Dr. Timothy Stenzel: Yes. So I don't, you know, bridging studies are done on the same sample but in - on different devices. You know, so - but it may be that you've already had some point of care studies done outside the US. And if it's, you know, through discussion with the FDA review team, if those are relatively closely mimic what a point of care site would be in the United States, you know, I'll leave it up to the review team to assess that.

But it could be that you add to what you already have; you don't necessarily repeat everything that we would ask for, in the US, that we would ask for, for a point of care study. So again, it's situational. The team will want to look into, you know, your technology; what you've done; and look at the sites that - and the characteristics, the sites where you did the point of care study, to assess that.

(Luis Jimenez): Thank you very much.

Coordinator: Thank you. Our next question comes from (Raymond Blay). Your line is open sir.

(Raymond Blay): Yes, hi. Good afternoon. For a prescription at home test would FDA grant authorization if mechanisms were not yet in place to report results back to the ordering healthcare provider?

Dr. Timothy Stenzel: So if it's by prescription there's automatically some relationship between the prescriber and the patient. They are somehow connected, right? And the reporting that we recommend but don't - let me say this. I mean we encourage - I think and usually the labeling of a test that we've authorized in this setting, we do suggest that the home test user relay their results to their clinician and discuss the results with them.

But the FDA has no way of enforcing that. And we don't make it a requirement for authorization of point of care tests and/or home tests that there is a mechanism prior to authorization, of reporting results. we do ask in the templates, what are your plans to allow that reporting?

The - we - and just so folks on the call know, there is a vast underreporting of point of care results in the US. And in home, home use tests. None, you know, anywhere in CLIA waived settings or at home. There's just a vast underreporting of that. And that's so important for us to help from a public health perspective, to help manage best this pandemic is to know what the, you know, what the results are from all those point of care tests.

So usually as a condition of authorization and to be handled post-market we get agreement from developers to find a way to make reporting possible. So hopefully that helps. Thanks.

Toby Lowe: And just to clarify Tim, I believe you're mostly speaking about reporting to public health authorities. In terms of reporting to the patient and the ordering healthcare provider, if it is a prescription test, we do expect the result to go to the ordering healthcare provider.

(Raymond Blay): So…

Dr. Timothy Stenzel: That can be done by phone. You know, that could be done by conversation or, you know, however the clinician and the patient decide.

(Raymond Blay): Just a quick follow up question. If for instance, tests were purchased by a university or distributed to students under some standing order from a healthcare provider, would it be acceptable for results not being shared with the prescribing healthcare provider for the university?

You know, I'm thinking about, you know, hundreds if not thousands of student doing testing with an at home test kit based on sort of a global prescription, if that makes sense.

Dr. Timothy Stenzel: So if you look at the tests that we've authorized, we make - there's labeling in there that suggests that results should be reported. If you're in a school setting, I think you want to know - the school wants to know those results. Right? So you want to know that - you're having them do testing for a reason. So, you know, as far as the details go, I don't know that it's under the purview of the FDA. It's more under the practice of medicine.

And that's governed more by state and local rules and laws. So what we ask for prescription tests is that they are prescribed and then we have our labeling that we authorize in the tests for suggestions on what to do. And there are flexibilities there. You know, someone is doing a blanket clinical order for testing, they can provide information in addition to what information you can get from the tests, in the test kit, or even the patient in healthcare provider fact sheets that the FDA posts online.

A prescriber can, you know, say hey, you know, if you're positive do this; if you're negative do this, don't do this, or whatever. So it's really up to the prescriber. Tests by prescription for this very purpose, have another mitigation that allows us to have a lower bar for prescription tests if a clinician is involved and can advise their patient, you know, about these things.

(Raymond Blay): Great.

Dr. Timothy Stenzel: So if you want to have a greater discussion on what might be acceptable on a college campus in their specific situation, I would suggest you send an email to the Templates email box and ask for Toby and Tim. And we'll arrange a call at the right level, to help you out.

(Raymond Blay): Super. Thanks so much.

Coordinator: Our next question is from (Josh Perfetto). Your line is open.

(Josh Perfetto): Hi. Thanks for taking my call. My question is about the interaction of the asymptomatic and pooling schemes for high complexity molecular testing. So if the use is going to be pooled testing of asymptomatic individuals, does that just require, you know, the asymptomatic and the pooling schemes to be validated as - in the template? Or would you somehow have to kind of like

actually do pooling of your asymptomatic samples when you're validating your asymptomatic testing?

Dr. Timothy Stenzel: That's getting into the weeds. But we certainly encourage a pooling. We think it's a great way to expand testing. It's a great - it's great if kit manufacturers validate pooling so that their customers don't have to validate anything themselves. They simply follow the pooling instructions in the authorization.

Pooling can be launched without prior - prior to an FDA authorization. So developers of a kit can validate pooling, you know, in launch and within Toby, 15 business days to submit - no, no, rather they have to submit but they don't have to have a decision on the pooling scheme. They can launch right away.

So make your - validate your pooling, submit it to the FDA, then you can launch. With asymptomatic we do want to see enough asymptomatic to know that the test is accurate, the conjoining of pooling and asymptomatic. Because if something's not authorized for pooling and there are no limitations - there are some tests, rare tests that are limited to symptomatic patients only, there's - we haven't given that limitation.

We're, you know, we're not objecting to prescriptions for off-label use by clinicians if they want to use a test that's authorized for asymptomatic. But it's really a question of asymptomatic pooling. I think, you know, that's best, you know, interacted with our team. But, you know, we're going to look at what are - from your particular tests what are the CT distribution of your asymptomatic population?

We're going to look at the CT distribution for your symptomatic population and we're going to look at what the impact of your pooling scheme is on CTs for positives that are pooled. And we probably can make an assessment about whether the data is adequate to be authorized. So it's a little bit hard to pre-judge, but once we have the data or you want to run a clinical trial or a clinical study and SOP bias, you can do that as well.

(Josh Perfetto): Okay. Got you. Thank you very much.

Coordinator: Our next question is from Laura Ferguson. Your line is open.

Laura Ferguson: Hello. Thank you for taking my call. Laura Ferguson with Delphine Diagnostics. And I have a question with regard to QPR test kits - QPCR. Are you - what is the current thinking with regard to the ability of these tests to detect the new infectious variants; highly infectious variants? Is there a requirement or current test under EUA review to demonstrate that they can detect the UK and South African and Brazilian variants?

And is there any requirement for tests that are already on the market, to demonstrate this? That is would new tests that have demonstrated that they can detect the new variants, are they able to state that to potential customers with regard to other tests that are already on the market, that may not have demonstrated their ability to detect these variants?

Dr. Timothy Stenzel: So, you know, we issued a safety alert around the variants. We described three tests that we saw that there was impact - potential impact based on variants. We describe that some - I think that from the beginning we've been asking developers to take a look at the sequence in the database and do an in silico analysis.

We would specifically call out anything that we know is in the database at a percent above 5%, especially in recent weeks and months. Because we see that as potentially even one mutation if it's 5% or above, could really degrade performance. And we want to know for our new submissions, know what the impact on the test is.

And we would also look to the known key important variants out there like South African, Brazilian and UK, and look at and assess performance. I can't pre-judge what our teams would say because there could be simply a limitation that says they can't detect the UK variant or it can't detect South African. But I think both of those are increasing rapidly in our population and would probably - if a test, a new submission could not detect those, it would put that submission at risk.

We do - I do recommend that - or I do encourage, not necessarily recommend, that all developers consider this. That all developers look at their assays now. But in the development of the assays that they look at this potentiality. And we know that assays that target multiple parts of the virus are going to - especially the multiple very conserve parts of the virus, are going to be less impacted going forward, by accumulation of more mutations than the virus and variants of importance.

We're, you know, we're looking to really share this surveillance activity on mutations with developers. We've been doing it for molecular tests from the very beginning. And we continue to look at variants - in variants - variants of relative frequency and also variants of importance like the three I mentioned, across all of the EUA-authorized molecular tests, because we have all the primer and probe sequences. They're proprietary sequences that we don't share.

And but we can run those sequences on a regular, on a weekly basis, through our database, and see if there's any tests that might pass that look like there might be a problem. We then assess that risk before reaching out to a given sponsor. Once we assess the risk and think it's high enough that we want the sponsor involved, we'll reach out to the sponsor and we'll put the sponsor on that.

So we issued the safety communication or alert, on variants. When we have new established information about any test that might be affected by variants, or mutations, we will as soon as possible, update our alert or notification of an additional test or tests that may be impacted. So this is a very relevant, timely thing that we're doing.

We've said before that it's very hard to assess the antigen and serology test. But we are endeavoring in inter-agency groups, to figure out how to do that. But we don't have a solution yet, for antigen and serology tests.

Laura Ferguson: Thank you.

Coordinator: This does conclude our question-and-answer portion of our call. I will now turn our conference back over to our host, Ms. Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions during today's town hall. Today's presentation and transcript will be made available on the CDRH Learn Web page at www.FDA.gov/Training/CDRHLearn, by Friday, February 26. If you have additional questions about today's presentation, please email CDRH-EUA-Templates@FDA.HHS.gov.

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

Coordinator: This does conclude today's conference call. We thank you all for participating. You may now disconnect. And have a great rest of your day.

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