Virtual Town Hall #82
April 6, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kimberly Piermatteo: Hello, and welcome everyone to virtual IVD Town Hall number 82 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in response to COVID-19. Thank you for joining us today. This is Commander Kim Piermatteo of the United States Public Health Service, and I am the Education Program Administrator within the Division of Industry and Consumer Education in CDRH's office of Communication and Education. And I'll be your moderator for today's Town Hall.

A recording of today's Town Hall and a transcript will be made available on CDRH Learn under the section titled Specialty Technical Topics, and then the subsection titled, Coronavirus (COVID-19) Test Development and Validation Virtual Town Hall Series.

The March 23rd IVD Town Hall recording and transcript have been posted. The next scheduled IVD Town Hall will take place on Wednesday, April 20th, 2022.

Our panelists for today are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health or OIR in CDRH's Office of Product Evaluation and Quality; Toby Lowe, Associate Director for Regulatory Programs in OIR; and Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices also in OIR.

For today's Town Hall, we'll begin with opening remarks, followed by answering your previously emailed questions, and then proceed to answer your live questions. I'd now like to welcome Toby, who will provide today's opening remarks. Toby, the floor is yours.

Toby Lowe: Thank you, Kim, and thanks everyone for joining our continuing series of Town Halls here. We do have a couple of updates, and Kim is displaying a slide that includes these new FAQs that I'll talk about.

On the last Town Hall, we mentioned this study conducted by Emory and the Children's Healthcare--Children's Hospital of Atlanta that looked at the validation data to support pediatric self-swabbing. So as promised on the last Town Hall, we have added an FAQ that includes this information and the master file number is included in the FAQ at that link. So any developer that's looking to leverage the data from this study can do so by referencing that master file number.

And then the second update, just posted maybe less than an hour ago, probably. And this is just an update. We've gotten a lot of questions on this Town Hall and in other venues regarding what happens to tests that are offered under EUA if the public health emergency expires and is not renewed.

So we've talked about that a little bit on this call before, and we did post this FAQ to help with that ongoing question. Essentially as we've talked about on this call, we definitely don't plan to take any action that would leave the American public without the tests that they need. And we recognize the need for an appropriate transition period.

It's also important to note, as we've talked about here before, the distinction between the public health emergency determination under section 319 of the Public Health Service Act, and the separate declaration under section 564 of the FD&C Act. And it's that second one that enables the issuance of EUAs.

So the public health emergency declaration for COVID-19 was issued on January 31 of 2020, and has been extended every three months since then. The public health declaration-- public health emergency declaration can expire if it's not extended. However, the EUA declaration under section 564 does not expire, and it is not dependent on the extension of the public health emergency declaration. The declaration-- the EUA declaration under section 564 continues until the HHS Secretary terminates it.

And many of the previous EUA declarations such as formers, Zika and Ebola, remain in effect, especially for in vitro diagnostic tests. So there's additional information on the website, including discussion about the transition guidance that we've talked about on the Town Hall before, which has been issued in draft, and that guidance proposes that there will be at least a 180-day transition period. And the FDA will finalize that guidance once we review the public comments on the draft.

So those are the updates for today. In a minute, we'll go into the questions that we received ahead of time, but I do want to note that we have received some questions that are a little too detailed or test or case specific to respond to on this call. And if we have not already responded by email, we will do so within a few days. And then we also continue to receive a lot of similar inquiries that some of them are appropriate for the Town Hall and we try to address them in the introductory remarks, such as the two topics that I just covered.

And then other ones are really not able to be addressed on this call because they are too specific. For example, we continue to receive numerous questions about which EUA molecular comparator is acceptable, and we welcome those inquiries at the templates email box CDRH-EUA-Templates@fda.hhs.gov.

And we also receive numerous questions about enrollment strategies and specifics of clinical study designs. And those really are best handled through a pre-EUA submission. So with that, I will hand it back over to Kim, and we can move into the questions.

CDR Kimberly Piermatteo: Great, thank you, Toby. So we'll now answer a previously emailed question about COVID test development and validation. So, Toby, the first question we have is, "there have been several COVID-19 test recalls recently for tests that were not FDA authorized, how can we check which COVID-19 tests have been cleared or authorized by the FDA?"

Toby Lowe: Thanks, Kim. So all FDA authorized tests are listed on the FDA web page. The slides for this webinar, typically include the link to the listing of EUAs. And so you can find that on the slides that are posted from these webinars, and also, I think probably everyone on this call is familiar at this point with where on our website the EUAs are posted.

We also have a risk specifically of FDA authorized at-home, over the counter COVID-19 diagnostic tests that can be found at the FDA's at-home, OTC COVID-19 diagnostic tests web page.

Regarding the recalls that have been posted recently, we do regularly monitor the safety and performance of COVID-19 diagnostic tests, including reports of adverse events and performance issues,

and also, the marketing of unauthorized, unapproved, or uncleared tests. And we issue safety communications to help educate test users, caregivers, health care providers, and generally the public to-- and to help reduce the risk of false test results that could lead to serious illness and death.

So only home tests that are authorized by the FDA should be used by the American public. And we take steps to remove unauthorized home tests or any inappropriately offered tests from the market and inform test users and the public, caregivers, health care providers, to avoid using those tests.

And we do want to emphasize that the use of inaccurate tests could harm our collective ability to stop the spread of COVID-19. So that is why we have been putting out those notices for those recalls.

CDR Kimberly Piermatteo: Thank you, Toby. So that wraps up our previously submitted question. We will now go ahead and take your live questions. So to ask a live question, please select the Raise Hand icon at the bottom of your screen. When you're called on, please follow the prompt in Zoom to unmute yourself, then identify yourself and ask your question promptly. A few reminders before we take our first question, please limit yourself to asking one question only. If you have an additional question, you may raise your hand again to get back into the queue and we will call on you as time permits.

And lastly, please remember, we are not able to discuss specific submissions under review. So our first live question is from James. James, I'm going to unmute you. Please unmute yourself and ask your question.

James Mullally: Hi, Tim, Toby, and Kris, this is Jim Mullally from MCRA that's M-C-R-A. I have a question regarding prior OTC test experience and study subjects for an OTC study. So given that many people in the United States have already had experience with home use antigen tests, excluding anyone who had prior experience from a study would present a recruitment challenge for an OTC clinical study.

And so I'm wondering if it's necessary to have an exclusion to include prior use of OTC antigen tests for study subjects in an OTC study? Or is it necessary to include any type of a washout period for prior use? Or is FDA accepting of studies where subjects can have some limited home use experience?

Timothy Stenzel: Yeah, thanks for this question, and you rightly point out a potential source of bias, and also rightly point out that it's hard to imagine someone in the country who hasn't had their nose swabbed or that there's that many people that don't know how to run home test now.

We're not looking to exclude those folks. What we are looking to do is eliminate bias at the time-- introduce bias at the time that the candidate test is being studied. And so if-- depending on how you're doing your study, there are potential sources of bias. There's also recruitment bias and enrichment bias.

So any time there's potential bias, we do recommend that you run your study and your selection enrollment and enrichment criteria bias-- if you're going to try to do that, first, in a pre-EUA way, in order to review and make sure that bias is eliminated or mitigated.

But in general, we would like when possible for the test subject to perform the candidate test first, and then the comparator test result. A sample will be obtained by whatever method you're looking to do. Any follow up questions on my response?

James Mullally: Yes, Tim, that's very helpful. I'd seen in previous FDA public comment that the clinical truth or the standard of care tests should be conducted first. And so if the study is recruiting those who are coming for COVID testing, how can the study be designed such that the candidate test is used before the standard of care test?

Timothy Stenzel: Yeah, that is our general recommendations. It's not a requirement. I think we depend on local IRBs and the submitter and the study designer to figure that one out. But if-- so there's a couple of possibilities.

There's the test of record is one of the tests we would allow as a comparator or it's not and you have another comparator. And so I would say, if it's important to do the test of record first, get that out of the way, then move into the clinical study domain, and then do the candidate test first, or you can randomize as well.

So that is an option for use here. And so it's unfortunately not something-- because there's different options here that we can only prescribe, and we wouldn't really recommend exactly how to do this because there's different ways to do this that are OK.

James Mullally: Great, thank you. If I could have one more follow up, it's directly related. If the sample type were different-- so if this the swab were going deeper into the nasal canal for the comparator, and that's the standard of care, would that be acceptable to collect first since the collection method would be different? In other words, if the standard of care tests were done first, that's also your comparator.

Timothy Stenzel: Yeah, well if that's the case, then that does-- there's less potential interference with an anterior nasal swab. But if the comparator's different, the comparator is mid-turbinate and the candidate devices and anterior nares and it's different than the test of record then, I think we'd prefer you did the candidate test swab first.

But also remember that if the candidate test is an anterior nares swab, you can use a comparator test that uses an anterior nares swab.

James Mullally: Great, thank you. Your feedback is very helpful. Thank you.

Timothy Stenzel: You're welcome.

CDR Kimberly Piermatteo: Thanks, Jim. Thanks, Tim. So our next question comes from Enes. Enes, I'm unmuting your line. Please unmute yourself and ask your question.

Enes Gunes: Hello, everyone. Thank you for this organization. Actually, my question is related to that-- the template for developers of molecular and antigen diagnostic for home use tests-- 9E and 9F, which means page 17 and 18 for records. Actually, it's written like PPA equals or higher than 80 in one paragraph, and the last sentence of this paragraph is like smaller than 95.

There are four paragraphs on this section, and a PPA lower than 95% should be limited to providing presumptive negative results is written. Actually we couldn't understand these differences, can you explain the differences between on PPA higher or equal to 80% and PPA lower than 95%?

Timothy Stenzel: Yeah, and we're talking about an antigen test here or a molecular test?

Enes Gunes: Rapid antigen tests. Not molecular.

Timothy Stenzel: Rapid antigen tests, OK. Alright. So rapid antigen tests, the ones that have been authorized under study conditions typically have sensitivities or positive predictive-- or present positive agreement in the 80s, sort of low to mid 80s.

We are looking for those tests to have at least an 80% sensitivity with say a minimum of 10% low positives. And that's sufficient for a rapid antigen test, as long as the NPA-- negative percent agreement or specificity is not too low.

We also have recommendations for NPA. So getting at or above 80% PPA, as long as all the other conditions of authorization are met, validations are OK. Then that should be sufficient for authorization.

And then-- and this covers molecular test as well. Sometimes molecular point of care tests aren't as sensitive as central lab molecular tests. And there are at least one that I'm thinking of-- there may be more that are below 95%.

So any time a test falls-- its performance is expected to fall below 95%, but above-- at or above 80% is still authorizable but if it's a point of care or home test, but it is-- or an antigen test, but there's an additional wording in the intended use that says that the negative results from such tests are presumed negative results.

Unlike tests that have-- these are classically molecular tests that have sensitivities above 95%. Most of those are central lab tests. That then-- they don't have that disclaimer that negatives are presumed negatives. It just says a negative result. Does that answer your question or questions?

Enes Gunes: Actually, thank you. I got the point. Thank you.

Timothy Stenzel: So you can just-- all the antigen tests have that disclaimer of the negative results are presumed negative. And a small number of molecular tests and point of care tests have that same language. And then of course, to put it into the current thoughts about performance of antigen tests, they are challenged by a number of things-- by variants, and other situations.

And so it is really best with an antigen test-- and when COVID is relatively prevalent and we're still seeing tens of thousands of patients a day test positive in the U.S. So it's still relatively prevalent, even though it's much lower than before. When you get a positive result with an antigen test, you should act on that as a positive result. If it's important to know for sure, somebody can always go and get a confirmatory molecular test. But if it's negative, and especially if you're symptomatic, that just needs to be interpreted with a lot of caution.

And, again, it's presumed negative and someone shouldn't assume that they don't have the virus, especially if they have symptoms and either a serial testing with the antigen test or potentially just going to get a molecular test to make sure you don't have COVID is what's in current labeling, OK?

Enes Gunes: OK, thank you. You mean that it doesn't create any very handicapped position for our test, right? If the—

[INTERPOSING VOICES]

--95%

Timothy Stenzel: Yeah, I don't know what you mean by handicapped, but we're just trying to reflect the real-world situation and the fact that antigen tests are less sensitive than molecular tests and you will have false negatives.

Enes Gunes: OK. OK, thank you.

CDR Kimberly Piermatteo: Thank you for that question. Thanks, Tim. Our next question is coming from Sam Ali. Sam, I'm unmuting your line. Please unmute yourself and ask your question.

Sam Ali: Yes. Hello, hi. Thank you for taking my question. I'm Sam Ali, from Intune Bio and the question is about a multiplex antigen test, we're planning to do a clinical trial for self-testing of SARS-CoV-2 plus flu A and B test, and just wanted to check-- I believe the FDA they have mentioned previously that you are accepting such applications and want to check on the minimum performance requirements in terms of the number of positives and BPA, MPA.

So in the template, I think it's mentioned that there is a minimum of 30 COVID, 50 flu A and 30 flu B, but I don't see any performance minimums in terms of percent sensitivity or specificity. And I think that the description in the template might be more related to POC and this is self-testing, there are many differences. So if you can please just give us some info that'll be helpful. Thank you.

Timothy Stenzel: Yeah, so I think I might start this one, and then let Kris finish it up. So let me just clarify. This is an antigen test. You want it to be a home self-test, and SARS-CoV-2 plus flu A and flu B?

Sam Ali: That's right.

Timothy Stenzel: OK. So we are currently open to receiving submissions in this category. More details will be needed to give you specific feedback, so we would like to know what is your plan? What is your study design? How are you going to source flu A and B, in particular?

There's actually a surprising amount of flu A circulating right now. And in fact, the positivity rate for samples tested for flu is-- the last I checked was around 7% in the U.S. And for SARS-CoV-2 was down, lower than that in many areas.

So if you're testing for flu, you might get more positive than if you're testing for SARS right now. But, unfortunately, there's very few flu Bs-- almost zero circulating right now. There were some minimal numbers circulating earlier in the respiratory season. So getting fresh flu Bs is going to be a challenge.

So you can come in with what you plan to do and a pre-EUA that's what I recommend and we can give you very specific instructions about what can be done to assist you in developing this test given the situation. One thing to consider is, is there a way and we've done this even for non-pandemic situations, some of the high multiplex panels, they may have a lot more targets on their panel than they submit-- have data to submit for their authorization to the FDA.

And those when they're molecular based, they can turn off the signal for analytes that they don't have enough data for to support a submission. But later on, they accumulate more data and they-- the FDA can authorize turning those channels on. It's a little bit more challenging with antigen tests, but it could still be done where you have an antigen test that gives you results for SARS-CoV-2, flu A, flu B, but somehow, mask those results.

There's certainly something that has to be instrument read and can't be visually read that can be done very easily. Something that's visually read more challenging, but it's still possible to mask the results for those flu A and B lines until you have enough data to support. So that's just an added aside about some of the challenges you're facing.

I think I'll stop there and see if Kris wants to pick up and more fully address some of your elements of your question.

[INTERPOSING VOICES]

Sam Ali: Yea, thank you, Tim.

Kristian Roth: Yeah, I guess with regard to performance, I think our expectations are going to be the same as there would be for a 510(k) for flu. So you can go back and look at those previous devices that were flu antigen tests, but you generally-- the same 80% bar compared to a molecular test is something that-- that's a pretty good precedent.

And then if your panel is adding SARS-CoV-2 to a previously cleared reagent for influenza, that maybe one set of considerations, but if they're both-- if all analytes have not been previously cleared that's maybe a little bit different as well. So if you are going to send in a pre-EUA it'll be important to make that distinction.

Sam Ali: Yeah. This is a new test. It's an ex-US sponsor, so it has not been approved previously. Thank you very much, appreciate it. Just to follow up a question, if it's not possible, for example, to get the 30 flu B, can the study continue post EUA and try to collect those numbers after the approval?

Timothy Stenzel: Yeah, that's what I was alluding to, yeah. Yeah, but we don't want in the interim, if you get an authorization for SARS-CoV-2, we don't want the users to be able to say, oh, I have flu A or flu B, or think they have flu A or flu B, that's the challenge. OK?

Sam Ali: Yeah.

Timothy Stenzel: It's a design challenge for you and the users seeing those results.

Sam Ali: Yeah, thank you. Thank you, I appreciate it.

CDR Kimberly Piermatteo: Thank you, everyone. Our next question is coming from Richard. Richard, I'm going to unmute your line. Please unmute yourself and ask your question.

Richard Montagna: Yeah, thank you for taking-- [AUDIO OUT].

CDR Kimberly Piermatteo: Sorry about that, Richard. I think that was my fault on my end.

Richard Montagna: How's that? Is that better?

CDR Kimberly Piermatteo: Yes. OK.

Timothy Stenzel: We can hear you. Yeah.

Richard Montagna: Thank you.

Timothy Stenzel: I was worried, thanks.

Richard Montagna: When the original wave of EUA authorizations came out, I think, virtually, all of the tests-- the PCR and PCR molecular test were authorized for use with people who were suspected of COVID-19 infections, and we're aware that many people are now going back in for asymptomatic claims. But we're also aware that many of these original tests that were not authorized for asymptomatic are just kind of being routinely used for screening purposes, whether they're drive thru's or whatever.

And we're just curious as to what FDA'S position on that. Are these off-label uses or is it being left up to the collection sites to decide how they use them? We're just curious as to your views on it. Thanks.

Timothy Stenzel: Richard, what organ-- what organization are you with?

Richard Montagna: I'm with Rheonix. We have an EUA for—

Timothy Stenzel: OK. OK. OK, thanks. Yeah, so I don't know that we still-- that we yet have enough permissions for asymptomatic screening for us to be satisfied that we have enough. And early on when there were none yet that had come in and there was a need for asymptomatic screening, we made the decision that we didn't want labs to turn away samples that were asymptomatic that they should be tested and reported out, even if the test they were using didn't have an authorization for that.

I'm going to turn to Toby and/or Kris to-- in a minute here to more fully explain that and more fully explain our current situation. But I think we understand that challenge and certainly we welcome continuing submissions for asymptomatic screening.

For any tests that already has authorization and has sufficient performance, they can get an asymptomatic claim at the moment without too much work through the serial testing plan. But the details, I want to turn to Toby and Kris on that but we certainly do still welcome that.

And, Toby, if you might go first here and fill out some of this information of the current status.

Toby Lowe: Yeah, absolutely. So, generally, those tests that were authorized for individuals suspected of COVID, they're authorized for individuals suspected of COVID by their health care provider. They're all prescription use tests.

So for those, it's really at the discretion of the prescribing health care provider, whether that is a personal physician or a health care provider that's-- excuse me, overseeing a larger organization or testing operation, making the decision on who might be suspected and depending on the prevalence in a community that might be anyone who's out and about in the community.

So that's sort of been-- as Tim was talking about there are not as many tests that are authorized for asymptomatic screening as there are tests that are authorized for individuals suspected of COVID. So that's really been left to the prescribing health care provider or the ordering health care provider that said as Tim discussed, there are tests that have been authorized for screening that have provided data to demonstrate performance in that population.

And so we do continue to encourage developers to seek out that indication because it will benefit all the testing programs to have more tests that are validated with individuals who are asymptomatic and not exposed.

Timothy Stenzel: Yeah, thanks, Toby and before I turn it over to Kris for any comments from Kris about this, there are some prescribers and institutions, new clinics and hospitals and labs that preferred it only used fully, everything's covered by EUA authorizations, and fortunately they have the choice. They can-- there are tests available that have those claims that they can use in those circumstances. And I've just checked with Kris and he doesn't have anything additional to say. So thanks for your question.

CDR Kimberly Piermatteo: Thank you. Our next question is coming from Ivan. Ivan, I'm going to unmute your line. Please unmute yourself and ask your question.

Ivan Brukner: Yes. Hi, can you hear me?

CDR Kimberly Piermatteo: Yes, we can.

Ivan Brukner: I would ask a general question for, how to say, home based devices. Like either their molecular tests, like nucleic acid base, like Cue or Lucira or Visby versus antigen assays. How come that nucleic acid assays have a sample internal quality control incorporated and you recommend it, while the enzyme immunoassays do not have?

Timothy Stenzel: Can you ask the last part of that question again? Why do molecular assays have what? And versus—

Ivan Brukner: In other words, you are controlling sample quality for nucleic acid base tests, which is fine—

Timothy Stenzel: OK.

Ivan Brukner: That's not for [INAUDIBLE] assay, which-- yeah. Is it-- is it obligation now? Or what is the—

Timothy Stenzel: I'll turn it over to Kris if he wants to expand on what I say, but the simple answer is that it's relatively simple for molecular assays to incorporate an internal control to make sure that an adequate sample is obtained or it's much more challenging for an antigen test to provide such a control.

And so that's where the state of the art is for molecular tests and the antigen tests haven't gotten there yet. That said, there have been circumstances where we have enough data, usually post market data, where we've removed the requirement for molecular-- say in a home collection, to have an internal control just because they have done so many tests showing that the internal control that their processes and procedures and their assay was so sensitive enough that the internal control didn't add anything.

So that's our general thinking about this, Kris. I don't know if you have anything to add about that.

Kristian Roth: No, I think that's where we are. Thanks.

Timothy Stenzel: Thanks for your question. And I will let everybody else in line know, I know that we have some people who haven't asked the question yet, and we have some people who have already asked a question and just in case it is not obvious, we internally have decided we want to make sure that everybody who has a first time question on a given call gets to be able to ask their question before we go back to those who are getting back in line.

CDR Kimberly Piermatteo: Yes, thank you for that, Tim. Alright, so then our next question is coming from Geetha. Geetha, I am unmuting your line. Please unmute yourself and ask your question.

Geetha Rao: Thank you. Thank you, Kim. And thank you Tim and Toby. I have an administrative question, and it's a follow up on a question I had earlier where I'm representing a company, SummerBio, and there is an LDT EUA that is now in process for an individual EUA and several months ago, I had mentioned the fact that the company is in the process of looking to relocate its facility.

And, Tim, you had suggested that we run that notification by FDA. So we have provided that notification, but we haven't heard back. And the relocation is very imminent. So I don't know if it's still OK for the company to go ahead and start offering the test in the new facility. The facility is just a couple of miles away. It's CLIA certified. It's gone through all the CLIA process requirements and all--

[INTERPOSING VOICES]

Timothy Stenzel: Yeah, Kris, is that was a question that you can handle?

Kristian Roth: I don't know. We've answered this before, but you know your EUA is likely under review.

Geetha Rao: It is. It's been triaged, as in the queue.

Kristian Roth: Right, and so I think if it does get authorized, it would be authorized for the new location. And as long as you have kind of notified us that it is a new location, that's something we would go forward with. I don't think that's going to affect the validation data requirements or data cut off or anything of that nature, just once you get the letter, it will have a particular address on there of the location that is current.

Geetha Rao: Right. My question is about what do we do in the meanwhile? Because the company is still able to offer the test.

Kristian Roth: I have to make sure Toby had a chance to weigh in.

Timothy Stenzel: Yeah, so let me just clarify. So you've submitted your LDT and now you're moving the location of where that test is being performed. It's the same exact test. It’s done the same exact way and no changes to it?

Geetha Rao: Well, a little more complicated than that. So the original LDT was I would say, grandfathered in from 2020. Then after the November 15 policy change, a notification was filed and as a result, we have a new number and it's under review. So we're just waiting on that. In the meanwhile, the company is able to continue offering the test. And there have been some other modifications have also been filed. So everything--

Timothy Stenzel: OK, got it. Got it. So we have all the data from the test that you're going to use at the new location?

Geetha Rao: That's correct.

Timothy Stenzel: OK. You can continue-- you can move to the new location. You've notified us of the move.

Geetha Rao: That's correct.

Timothy Stenzel: When we authorize you-- that location will go into the authorization.

Geetha Rao: That's correct. The file itself has all the information and all the amendments to that like the address change and all that is in there. And any and all the modifications--

Timothy Stenzel: OK, perfect.

Geetha Rao: --since the 2020 version have also been filed. Everything is up to date, in terms of the FDA notification. We just haven't gotten any response yet. So--

Timothy Stenzel: Yeah, apologies about that. We're still getting swamped with a lot of EUAs. And we would typically probably only ask questions when we need an answer. And-- yeah, so based on the November 15 policy, 2021, you've notified us. You've provided us with the data. You're able to stay on the market. You can move the location of that, as long as you notify us and-- this is all done and in order to not contract the testing opportunities out there for the American public. So thank you for what you're doing and thank you for checking with us. I really appreciate it. Toby, do you have anything else to say?

Toby Lowe: No. I think-- it sounds like it's the same laboratory entity just moving physically. So that's not-- I think I agree, Tim, with what you outlined there.

Timothy Stenzel: Alright, thanks for checking.

Geetha Rao: Yeah, this is really, really helpful. So thank you so much.

Timothy Stenzel: You're welcome.

CDR Kimberly Piermatteo: Thank you, everyone. Alright, so our next question is coming from Neda. Neda, I'm unmuting your line. Please unmute yourself and ask your question. Neda, are you able to unmute your line?

Neda Savic: Hello.

CDR Kimberly Piermatteo: There you go.

Neda Savic: OK. Oh, great, you can hear me. So, hi, my name is Neda Savic, I'm from BioLytical in Vancouver, BC. We're currently developing a protocol for serial testing of asymptomatic subjects and we would like to know how many times the subjects need to come in for testing, at what time points, and do they need to remain asymptomatic for the entire duration of the study?

Timothy Stenzel: Alright, do you already have an authorization for symptomatic or is this a new test?

Neda Savic: We have it authorized for symptomatic.

Timothy Stenzel: Oh, and you're adding asymptomatic. Or is this the post-market commitment that the study-- that's in your original letter? No. Do you have a serial testing claim already and you're looking for data to support it after your authorization, or you're looking to add asymptomatic screening to your test?

Neda Savic: We're looking for post marketing.

Timothy Stenzel: Ah, post market study. So if it's in your letter of authorization-- well, this might be a question that's best handled through the templates email box. If you could send your question into the templates email box and ask that it be forwarded to Kris-- sorry, Kris and Tim, we'll get the details from you and be able to provide you with a little bit more directed approach on this, OK?

Neda Savic: OK. Thank you.

Timothy Stenzel: Alright, thanks.

CDR Kimberly Piermatteo: Thank you. Our next question is coming from Tianyang. Tianyang, I am-- I've unmuted your line. Please unmute yourself and ask your question.

Tianyang Liu: OK. Thank you. So my question is that we have an EUA authorization for the OTC test for COVID, and we are considering to develop the multi panel, which is COVID plus flu A and flu B. And we just want that per FDA's request, is it must be in one cassette, or it could be for three cassette?

And for the flu test, could we white label someone who has already got the FDA clearance for flu A and flu B, so that we will have a three cassettes in one box kit, and then could test three different kind of virus?

Timothy Stenzel: I think you're asking, can you put two or three different separate tests, one for SARS, one for flu AB, one for something else together in the same box and call it a multiplex?

Tianyang Liu: Yeah.

Timothy Stenzel: And get an EUA authorization for it?

Tianyang Liu: OK, so--

Timothy Stenzel: Or is that what you're-- is that what you're asking?

Tianyang Liu: Yes that's what I'm asking, yeah.

Timothy Stenzel: Are the non-SARS-- are any of the tests already authorized by the FDA?

Tianyang Liu: Yeah, both the COVID test OTC is authorized, and also the flu A and the flu B, all of the three are.

Timothy Stenzel: So all three tests are authorized, but we have not authorized a flu AB OTC test. So would this be for home use?

Tianyang Liu: That is for POC, sorry.

Timothy Stenzel: Right, so are you targeting POC or is this home?

Tianyang Liu: Yes, POC.

Timothy Stenzel: Oh, POC. OK, so the non-SARS tests are fully-- are cleared by the FDA for point of care, and the SARS test is authorized as an EUA. OK, so all these tests are fully authorized for their respective analytes.

So I'm just going to say in general, that I would recommend that you send an email to our templates email box, and you ask specifically for Toby-- sorry, Toby-- and Tim to see the email and give us some details about what you want to do so we can confirm this.

But in theory, if everything-- if three tests are-- or two tests are EUA authorized or are otherwise fully authorized, putting them together is something you can talk to us about. We often get questions about whether unauthorized tests that are separate could be submitted under one EUA and you're not asking that. But please submit your specific questions with the details-- to the templates email box, address and ask for Toby and Tim, OK?

Tianyang Liu: OK, thank you.

Toby Lowe: And just-- I just want to add, generally, you mentioned something about white labeling. If your white label-- if you're looking to white label someone else's test, you do need to work with that other entity to get-- to work on that arrangement and get a right of reference and become a distributor of their test.

Tianyang Liu: Yeah, we know. Thank you.

Toby Lowe: OK, great.

Timothy Stenzel: Yeah, Toby, that's good to ask. I made that assumption, which is not always good. Alright.

CDR Kimberly Piermatteo: Alright, thank you, everyone. Our next question is coming from Stacy. Stacy, I've unmuted your line. Please unmute yourself and ask your question.

Stacy: Yes, thank you. Hi, this is Stacy [INAUDIBLE] from Thermo Fisher Scientific. Firstly, thank you so much to the FDA panel for their support in this forum. My question pertains to transitioning EUAs and the clinical evidence needed to support a 510(k) for a molecular diagnostic. Specifically, will a prospective clinical evaluation study, meeting 510(k) criteria that was conducted to support an EUA, be acceptable for a 510(k) application having used an EUA assay as the comparator? Or will the FDA require additional clinical validation data to support the transitioning EUA to a 510(k)?

Timothy Stenzel: This is going to be a question I hand over to Kris because we were wanting to be able to pool data as performed and in your current EUA labeling, and so we would like to find a way to do that. And this may require offline communication with you about the details.

But we are looking to fill the gap between EUA and full authorization to make maximum use of the EUA submission data. Kris, do you have—you may like the idea of a pre-submission in this case? Not a pre-EUA, but actually a pre-submission for full authorization to ask these questions, but do you have anything else to add right now?

Kristian Roth: So if you've got prospective data already for your EUA, that's something that is mentioned in the special controls for molecular tests for SARS-CoV-2, which are-- were promulgated last year. Our recommendations for the comparator method are a little bit different in the EUA world versus the 510(k).

In EUA, I think we take a single EUA comparator method, 510(k) will take, I think we're recommending three methods to make sure that those positives are really true positives. But like Tim mentioned, we do want to make sure we're leveraging as much data as possible. So I think that's the right path forward would be letting us know what your plans are, what your existing data set consists of, and then asking that question in a pre-sub and we'll be glad to answer it in that format.

Stacy: OK, thank you so much.

CDR Kimberly Piermatteo: Thank you. Our next question comes from Ron Domingo. Ron, I have unmuted you line. Please unmute yourself and ask your question.

Ron Domingo: Hi, thank you. I'm working with a client right now who has an antigen test and this is related to the low prevalence of flu rates in the country right now. What strategies would the agency recommend to obtain the necessary five fresh samples for flu A and B in the season to support a multi-analyte test for an EUA? Thank you.

Timothy Stenzel: But this is an antigen test or a molecular test?

Ron Domingo: Antigen.

Timothy Stenzel: Antigen little bit more difficult. Yeah, an antigen a little bit more difficult because they usually use a direct swab and that's the best way to run those tests. So first of all, as I mentioned earlier in the session today, we are seeing in many areas rates of flu A positivity above SARS-CoV-2 positivity at the moment, which is unusual for the pandemic, but not necessarily surprising.

It's a bit late for flu but you know everything's sort of helter skelter in this pandemic. But as far as enrichment strategies to try to do that, at the top of the hour our talk of the session, Toby did mention

that if you want to discuss enrichment techniques to sort of find ways to find those samples, you can discuss that with us directly.

And please propose something that we can in a pre-EUA that we can review and comment on. But that's really the best way to handle this knowing that specificities of your device and what your current thinking is about how you're going to do that. One of the challenges as I mentioned earlier in this session is that there's almost no flu A-- flu B here.

So there is the possibility of using-- if you have an antigen test, of using banked swab samples, but, unfortunately, there's banked flu A and B direct swabs are unlikely to be plentiful or available. It's just not what people have done in the past.

So and then I did, I did mention earlier in this session and it'll come out in the transcript when the transcript is released, you know, about turning off the flu A-B signals if you don't have enough flu A-B for your submission that you want to submit your SARS-CoV-2 test before you have all your data for flu A-B. Toby, just anything else to add?

Toby Lowe: Not from me.

Ron Domingo: OK. Thank you, Tim.

CDR Kimberly Piermatteo: OK, thank you. We have time for one more question today. Engin, I am unmuting your line. Please unmute yourself and ask your question.

Engin Narinc: Hello, everyone. I am Engin from [INAUDIBLE] may clarify for me. My question is after the [INAUDIBLE] and clinical validation, approximately, what [INAUDIBLE] process take? Or if they approve of [INAUDIBLE] even though we have perfected the process completely?

CDR Kimberly Piermatteo: Engin, we're having a hard time hearing you. Can you speak a little bit louder and slow down a little bit?

Engin Narinc: OK. So sorry. Now we are managing a clinical validation process, and we are finishing today or tomorrow. Just a moment after this process and after documentation [INAUDIBLE] 100%. How much do we time for evaluation by FDA? By the way, so sorry for my English level. I am trying my best, but my English level is [INAUDIBLE].

Timothy Stenzel: Let me clarify your question. I think you're finishing up your clinical evaluation, and you're thinking of submitting your EUA in the near future. And you want to know estimated review times by the FDA?

Engin Narinc: Yes. Yes, of course.

Timothy Stenzel: OK, and is this a molecular test? Is it an antigen test? Is it a central lab test? Is it a point of care or over the counter?

Engin Narinc: It's an antigen test.

Timothy Stenzel: Is it a home antigen test?

Engin Narinc: Yes, home antigen test, yes.

Timothy Stenzel: OK. Alright, well, we are trying to currently move good antigen tests that those are submissions that are complete. We do an assessment after a test arrives, is whether the submission is complete or not. When possible, we give a fair amount of detail in our assessment of the application at that time if there's any deficiencies. And then we expect you to satisfy all those deficiencies for us to be able to pick up the review of the package and then we make a decision.

So bottom line is, submissions that are well done, that is the studies are clear, the results are clear, studies are favor authorization, and we have few if any questions of you, about how you've done things. And so the submission should be well organized and well written. So that we can find everything easily and we understand everything easily. When something like that happens and we're aiming to get those reviews done as quickly as possible. And those are the ones that go through really quickly.

The ones that have challenges for us and continuing challenges for us, we are going to take more time to make sure we make the right decision.

Engin Narinc: Thank you so much.

CDR Kimberly Piermatteo: Alright. Thank you, Engin. That was our last live question for today. And thank you to all of our panelists for providing their feedback. We really appreciate everyone's participation.

So as I mentioned earlier, a recording of today's Town Hall and a transcript will be made available on CDRH Learn. Please visit CDH Learn, at the link provided on this slide.

You will find the recording and transcript under the section titled Specialty Technical Topics, and then the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series.

For additional questions about today's Town Hall, and COVID-19 IVD topics in general, please email CDRH-EUA-Templates@fda.hhs.gov.

Lastly, please remember to join us for the next IVD Town Hall scheduled for Wednesday, April 20th, 2022. This concludes today's Town Hall. Have a great day.

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