Virtual Town Hall #81
March 23, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kimberly Piermatteo: Hello, and welcome to virtual IVD Town Hall number 81 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 Kimberly 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. 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 the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series.

The March 9 IVD Town Hall recording and transcript have been posted. The next scheduled IVD Town Hall will take place on Wednesday, April 6, 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 address your live questions. I'd now like to welcome Toby, who will provide today's beginning opening remarks. Toby, the floor is yours.

Toby Lowe: Thank you, Kim, and thanks everyone for joining us again today. I have a couple of announcements to make. The first is that recently there was a pre-print published for a study conducted by Emory University and Children's Healthcare of Atlanta, with support from the NIH, regarding the adequacy of nasal cell swabbing for SARS-CoV-2 testing in children.

This is a study that some of our SMEs from our team here were also involved with. And the clinical performance from that study demonstrated that children aged 4 to 14 can provide adequate anterior nasal specimens for SARS-CoV-2 detection when they're presented with age-appropriate instructional material, which included a video and a handout at a single time point. Emory University and Children's Healthcare of Atlanta have granted a right of reference to any developer looking to include pediatric cell swabbing for their COVID-19 tests that-- those developers can leverage the performance data and specimen collection protocols from the study on pediatric self-swabbing. And they've submitted this data to FDA in a Master File. So any developers that are interested in leveraging this information should reach out to their lead reviewer. And we will be putting information about this up on our website in the FAQs as well.

The second announcement that I wanted to share is that we recently put up a safety communication regarding-- as well as a couple of FAQs regarding the use of at-home COVID-19 tests and the need to use them properly, according to the manufacturer's test instructions, in order for them to continue to be safe and to avoid potential harm.

As noted in the safety communication, we have received some reports of individuals using them inappropriately, mistaking the vials of reagent for eye drops, or children getting a hold of them and drinking the solution. So obviously, these are not ideal situations, and we have issued the safety communication just to add some clarity there and to remind people to keep the tests out of reach of children and pets, and to follow the manufacturer's test instructions.

And along with that safety communication, we put out an FAQ about the safety of at-home COVID tests and the potential toxic chemicals. And we also put up an FAQ about expiration dates for home COVID tests. And with that, I will hand it over to Tim.

Timothy Stenzel: Thank you, Toby. Welcome, everyone. I wanted to briefly cover the topic and some areas of conversion of EUAs to pull authorized versions, with a special emphasis on antigen tests, since we have now granted a molecular test, and then followed that with a 510(k) of a molecular test. And so essentially, all molecular test follow-ons will, for point of care laboratory use, can be handled through the 510(k) process.

Where that's not available, then De Novo pathway is the process. And for the first successful submitter, all subsequent submitters will then be authorized under the 510(k) pathway. We don't know and we won't announce when we get De Novo applications or 510(k), and we don't know even if some of these first in-- whether they will be first out. It depends on the package and whether any additional work may be needed. So I do encourage and recommend that full authorizations be sought.

And for antigen tests, the recommendations for full authorization, whether it's De Novo or 510(k), are essentially the same. The first one-- that's a De Novo-- we do go into more work, because we write special controls, a document that outlines a method of down-classifying, and ways to down-classify, and reasons to down-classify because of mitigations to a 510(k). And so there is a bit more work for the FDA on the first application.

But essentially, the sponsors-- submitters of these full authorization packages all do the same thing. So the first one in for antigen will use molecular comparators, and the second one that's a 510(k) will also use molecular comparators. So we are able to provide recommendations, at least through the Pre-Sub and Q-Sub process for COVID test full authorization conversions.

So go ahead and get in, get in line and start understanding that from that point of view. But I did want to make it clear that there's really nothing different between the first De Novo and the second 510(k), for any of the areas as far as what our recommendations are for full authorization. The testing, the validation is essentially the same.

I would say also that, especially those that are planning to do EUA studies now, whether it be antigen, molecular, or serology-- well into the third year of the pandemic, if you're doing that now, presumably you want to stay on the market for a long time. And therefore, I would recommend that you, while you're doing your EUA studies, consider continuing those studies after you get enough data to submit for an EUA and collect for the full authorization.

It just seems relatively efficient for you to do that, rather than start something, stop it, and then have to restart later. So something to consider-- it's something that I would recommend, but it's certainly not a

requirement. It just seems to make sense at this time in the pandemic on when we're encouraging all EUAs to go ahead and perform their conversion studies.

Alright, and there's no time like the present to get that started. In all likelihood, we may see a slight resurgence in COVID in the coming weeks and months, so the number of positives should increase. If old patterns hold, we're seeing resurgent omicron BA.2 in Europe. And we're just anticipating, because of past historical patterns, that we'll see that here too.

With that, I'll turn it back over to Toby for her to respond to the pre-submitted questions. Thank you.

Toby Lowe: Thanks, Tim. And we can get started with the questions that were sent in now.

CDR Kimberly Piermatteo: Great. Thank you, Tim and Toby, for those opening remarks. We'll go ahead and we'll now answer your previously emailed questions about COVID test development and validation.

Please note, we received some questions that are too detailed or test case-specific that we will not be able to address during today's town hall. For those questions, we will try to send a response in writing within a few days. If you have submitted a question and you do not hear it addressed today, please look for a written response. If you do not receive a response within a few days, please feel free to reach back out to the CDRH EUA templates mailbox. So that's CDRH-EUA-Templates@fda.hhs.gov for an update.

Now let's get to the questions you sent in advance of today's town hall.

Toby, the first question that we have is, should a test developer notify the FDA of an additional manufacturing site or a different manufacturing site for an authorized test?

Toby Lowe: Yes, we do recommend that test developers notify FDA of manufacturing site changes. And you can do this by sending an email to your lead reviewer, and copy the email address that is specific to your EUA number.

CDR Kimberly Piermatteo: Great. Thanks, Toby. Our next previously submitted question is, do laboratory-based qualitative serology tests require an EUA?

Toby Lowe: Yes. FDA does generally expect newly offered COVID-19 tests, including LDTs, to have an EUA or a traditional marketing authorization, such as a granted De Novo or a cleared 510(k), prior to clinical use. And you can refer to the November 15, 2021 update to the COVID-19 test policy guidance for additional details. And that is linked on the slides that is showing right now.

CDR Kimberly Piermatteo: Alright. Our next question is, to support a 510(k), are reagent stability studies required to be conducted with panels of samples derived from natural clinical matrix?

Toby Lowe: Yes. Reagent stability studies should be prepared by spiking negative clinical matrix with inactivated SARS-CoV-2 at an analyte concentration of three to five times LOD, limit of detection. We do not recommend using recombinant protein.

CDR Kimberly Piermatteo: Thanks, Toby. Our next question has two parts. The first part is regarding transition. as discussed in the recent EUA transition guidance, will FDA accept supplements to existing EUAs after the FDA stops accepting new EUA requests? The second part of that question, is for

authorized tests, will the FDA expect developers to continue routinely monitoring and evaluating the performance impact of SARS-CoV-2 viral mutations?

Toby Lowe: Yes. So we do expect developers to continue routinely monitoring and evaluating the performance impact of SARS-CoV-2 viral mutations for as long as the test is being offered. This is included as a condition of authorization for all COVID-19 test EUAs. And we also expect this to be done for tests that receive full marketing authorization through a De Novo or 510(k). And we've included this in the special controls for the COVID-19 molecular test De Novo that was granted last year.

Unless revoked, EUAs are in effect until the declaration that circumstances exist justifying the authorization of the emergency use of In Vitro Diagnostics for detection and/or diagnosis of COVID-19 is terminated, and should be-- and those EUAs should be maintained in accordance with the conditions of authorization. Termination of a declaration that circumstances exist justifying the authorization of emergency use does not typically happen for quite a while, as can be seen by the previous public health emergency declarations that still have not been terminated, such as Zika and Ebola.

Regarding the transition guidance, transition plan for medical devices issued EUAs during the COVID-19 public health emergency-- that has been issued in draft for comment, and not for implementation. If there are points about the guidance that are unclear, we recommend that you submit a comment to the docket indicating areas that could benefit from added clarity. And if you have questions about how to manage your current plans for moving forward now with your emergency use test or with the 510(k), please send an email to the EUA templates mailbox with sufficient details so that we can provide appropriate feedback.

And notably, as Tim discussed as well, we have granted a De Novo and cleared a 510(k) for COVID-19 molecular tests, and we welcome additional 510(k) submissions for molecular tests. And while we have not yet granted full marketing authorization for antigen or serology tests, we are interested in doing so, and a De Novo would be the first step for each of those.

CDR Kimberly Piermatteo: Thank you, Toby. Alright, our next question is, do test developers need to evaluate the stealth omicron variant?

Toby Lowe: Yes. We expect developers to evaluate the impact of all relevant variants. The BA.2 variant-- which some have referred to as the stealth omicron, since it does not have an S-gene dropout-- has accounted for about 23% of COVID-19 cases in the U.S. from March 6 through 12, according to the CDC. We recommend assessing the prevalence of viral mutations in sequence databases, such as the GISAID database, as mutations observed in these databases at a significant frequency may signify that the mutation is present in an increasing proportion of infected individuals in the U.S.

And we currently consider a significant frequency to be greater than 5% when considered-- when considering at least 2,000 sequences over a recent period of time, such as the past week, month, or quarter. And additional discussion about that can be seen in the viral mutations guidance. And if you have specific questions about your test or about evaluation of specific variants, we recommend that you discuss that with your reviewer.

CDR Kimberly Piermatteo: Thank you, Toby. Our last previously submitted question is, is the NIH ITAP program still up and running? And have there been any recent EUA authorizations through that program?

Toby Lowe: Yes, the NIH ITAP program-- the Independent Test Assessment Program-- is still active. We have added the link for that program to the slide that is showing now. If developers are interested in the ITAP program, they can reach out directly through that link. And all EUA authorizations are posted to our website following authorization.

CDR Kimberly Piermatteo: Great. Thank you, Toby. That wraps up the previously submitted questions. We will now move to the live question and answer part of today's town hall.

To ask a live question, please select the Raise Hand icon at the bottom of your Zoom screen. When you are 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 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 again as time permits. And lastly, please remember, we are not able to discuss specific submissions under review.

Our first live question is from Phil. Phil, I'm going to unmute you. Please unmute yourself and ask your question.

Phil Groom: Hi, yeah, this is Phil Groom from Bond Digital Health in the UK. I have a question relating to test result reporting. So is there a necessity that results reporting will be required when companies convert to a full 510(k) authorization? And if so, will it be incumbent on the companies to provide a mobile phone app or website to users?

Timothy Stenzel: So I will let Toby and/or Kris weigh in on this. It's not something that I know right now we would advise. I know what we would want is that, because we are asking for connectivity, at least result reporting options for point of care and for at-home tests, that we would hope that those would be carried out into the full authorizations as well, given the public health importance of seeing that. Toby, Kris, do you have anything else to add at this point? This may be a good question for a Q-Sub, but I'm going to turn it over to you.

Toby Lowe: Yeah. So we haven't authorized under full marketing authorization a home test for COVID yet. And lab-based tests-- the lab is recorded-- is required to report. So the reporting for the labs is required under provisions that FDA is not responsible for. And we do encourage for home tests that reporting be built in. It is not required reporting under the same provisions as lab-based reporting, but it is very beneficial for public health, and we would continue to encourage that reporting mechanisms be built in for home tests.

Kristian Roth: Yeah. And maybe I could just add one thing. This is Kris. If you take a look at the special controls for the molecular 510(k) from BioFire that was granted last year, there is no mention of reporting in those special controls. So at least for that-- for 510(k)s under that De Novo, there's no requirement placed by FDA, at least. Thanks.

Phil Groom: Thank you.

CDR Kimberly Piermatteo: OK. Thank you, Phil for that question. Our next question is going to come from S. Hart. I am a meeting your line now. Please unmute yourself and ask your question.

Sue Hart: OK. Thank you. This is Sue Hart from Hemex Health. I have two questions. The first question is regarding an antigen point of care EUA request. We had a problem with our clinical study regarding the PCR comparator. It turned out not to be EUA authorized. We have in progress a home test submission we're doing, and we have that study completed. Could we use that clinical study for our point of care submission?

Timothy Stenzel: Yes. In short, yes. And in fact, we do recommend that those developers who are willing to take a risk-- we encourage the risk to go right to OTC studies, because if we issue an EUA for an OTC test, it automatically qualifies for a point of care without having to do any point of care studies-- specific studies.

All the studies that would-- that are important for point of care, are down there right with-- for the OTC version. It does save effort to do that. As long as the test performs fine in that OTC setting and all the other studies are done to support that, then that's fine. And we'd be happy to issue both a OTC version and a professional version of the test with-- solely with the OTC studies.

Sue Hart: My question is a little different. For reasons that are specific to our company, we want to submit both an OTC and a POC EUA request. And I don't want to go into what specifics regarding our company. Could we put the OTC study itself into a POC submission in addition to submitting an OTC request?

Timothy Stenzel: Yeah. That's what I was trying to say, that you can use the OTC study to support the point of care version of the test.

Sue Hart: OK. OK, great. And how would you handle the operator-specific questions in a POC submission? We have those questions answered for the POC study, but we would not submit the POC clinical data in that case, or just not answer it?

Timothy Stenzel: Right.

Sue Hart: OK.

Timothy Stenzel: Yeah, just explain everything in your submission. You can make two separate submissions, but do tell us that the two submissions are linked via the clinical study.

Sue Hart: OK.

Timothy Stenzel: You would have also done guard band testing for variable factors. I don't know if you did find a duplicate. It's probably a single kit used for both. How much can the time vary—

Sue Hart: Yeah, yeah. Yeah, yeah.

Timothy Stenzel: --when you're running tests. So just to make sure that, when you submit one or the other, or both at the same time, you provide cover letters that explain the relationship, and in the point of care submission, that you explain, that you're submitting all the point of care data that you collected

except for the clinical study. And the reasons why you're not submitting the clinical study data-- typically, if you perform studies, especially correctly, we want to see the data nevertheless. OK?

Sue Hart: OK, great. And then my next question is, if you happen to have a rejected EUA submission because of problems or whatever, could you resubmit a brand new EUA request once you've fixed everything?

Timothy Stenzel: Yes. Yeah.

Sue Hart: OK.

Timothy Stenzel: So we have a number of decline letters, depending on the specific situation. But if we issued either what's called a refuse to accept because the application wasn't complete in some way or we issued a decline to issue letter-- and the specific words are used in those letters, even though it's a little bit hard to sometimes decipher-- but if we had issues with the submission and provided feedback, and then, when we-- if we got a response, if it was inadequate, we would have gone ahead and declined to issue.

But yes, if you later on are able to address all our concerns, you're welcome to resubmit. And we would ask that you specifically address those concerns based on our prior communication with you specifically so we can determine whether or not you have addressed all of these issues.

Sue Hart: Wonderful-- thank you very much.

CDR Kimberly Piermatteo: Thank you, Sue. And thank you, Tim. Our next question is coming from James. James, I am unmuting your line. Please unmute yourself and ask your question.

James Mullally: Hi, Toby, Tim, and Kris. This is Jim Mullally from MCRA. That's M-C-R-A. I am representing Ravgen Inc, who is planning a combined usability and clinical study. And my question regarding that is whether FDA considers the main challenges to this approach-- having a combined usability and clinical agreement study-- from a validation standpoint, to be the introduction of potential training bias. And if so, can this be mitigated by having the subject conduct the clinical agreement study portion of the test first, and then doing the usability study portion?

And two is the other issue, identification of significant issues that could render the clinical study null and void. Should labeling changes be required, or are there other challenges that FDA sees?

Timothy Stenzel: So the main risk, Jim, is that you find out in usability study that you have to modify something. Right?

James Mullally: Yes.

Timothy Stenzel: Workload instructions that are significant that would invalidate the clinical study. Thank you for appreciating the potential for bias and doing the clinical study first, and then the usability-- to show the usability of the test seems fine. I know of no issues why you can't take that risk if you're willing to, because it obviously does save time and resources to do that. But Kris and/or Toby may have some additional comments to make on this.

Toby Lowe: Yeah.

[INTERPOSING VOICES]

Timothy Stenzel: Oh, go ahead, Toby.

Toby Lowe: Yeah, I would just say that, if you have specific questions about the study protocol, you may want to submit that as a Pre-EUA. But otherwise, I think Tim covered our general thinking there.

Timothy Stenzel: Yeah, I'm just telling you what-- if I was in your all's shoes, what I would do. First of all, if the test has been launched outside the U.S. and you have a lot of experience already with it, and it works fine, the risks may be lower. But if this is a brand new test-- you're coming first to the U.S., say-- and you don't have as much experience, then you may want to do some mini usability, mini clinical study to make sure that performance with those instructions is decent on a very small subset of users, even company personnel, just to verify that everything's-- that would mitigate some of the risk, obviously, if you did something that. But it's not required, not necessarily even recommended. It's just—

James Mullally: Right.

Timothy Stenzel: --something that, if I was in your shoes, I'd want to make before-- ensure before I went to this big study that everything seems to be working fine. But I've also done that, and it's not worked out either. [LAUGHTER] And it required a redesign and a new clinical study. So those of us who have been in the field a while know the challenges we can sometimes see. And we make risk-based financial decisions all the time.

James Mullally: Great-- yes. Thank you so much. I agree. And this has been very helpful.

CDR Kimberly Piermatteo: Thank you. Alright, our next question is going to come from Annie. Annie, I'm unmuting your line. Please unmute yourself and ask your question.

Annie Wright: Yes, hello. Thank you so much for taking my call-- Annie Wright from [INAUDIBLE] USA. Just like the previous caller, we had a EUA submission that was closed because part of our clinical data was rejected based on the RT-PCR that was being used. So we plan on resubmitting. So the remaining data that we have-- we basically have all 30 positives required, so we would only need to do the negative samples to supplement that.

But we were wondering about the sequencing that is required. Originally, in the first submission, they told us to submit 10 positive sequences for the omicron variant. So if we resubmit and we use the part-- the data that we had previously, can we still just do 10 for sequencing, or do we need to do 30 plus additional positives-- more than 10?

Timothy Stenzel: Yeah, so I'll just take it as an opportunity to remind folks that the FDA does recommend that you check with us about your comparator assay. There are clearly some nuances there. We want to make sure that it's an acceptable high-sensitivity comparator assay ahead of you doing the study so that this sort of thing doesn't happen. It's why we make that limitation. And re-submission after correcting that is fine.

As far as the sequencing that we have requested, this specifically has to do with omicron and performing-- and assessing performance in omicron, since-- because of some of the challenges that we've seen with omicron. So typically, if a submission has already been in-- and this time period is a little bit past now, because omicron is now obviously on the downswing, they may come up a little bit with BA.2.

For submissions that were already in, we were-- in order to speed them through the system, we were asking for a minimum of 10 samples that were from the omicron period to be able to assess performance. We weren't necessarily requesting a sequence analysis on those 10 pre-authorization, but the sequences could be potentially provided after if it was important to timely make the decision on the test.

And now, if you're doing the study anew, during the omicron period, we would ask that the positives be sequenced. It may be that you can discuss it with the reviewer, whether it's maybe the first 30 positives, and-- if there's challenges with getting sequencing back in a timely manner, and we have a subset, that's something else you can discuss with your reviewer as well. We're just trying to establish either pre-market or post-market performance on omicron samples. Kris, do you have anything else to add and suggest that this is something that often we want to have a dialogue about specifically for your situation? Go ahead, Kris.

Kristian Roth: Yeah. No, I think that's the point. I think we want to have a dialogue about it as we move forward in time. Obviously, omicron is predominant by quite a bit, so there may be other strategies we can take advantage of as well. I'd say don't hold up your submission. If you don't have that sequencing data, submit it and then start that dialogue with us so we can engage with you.

Annie Wright: OK. So essentially, we can use our previous pre-omicron data for the resubmission? And then we can basically submit it, and then once we address all the other issues, and then basically point that out and can we also, because the project is closed, can we contact our previously lead reviewer to ask her these specific questions? Is that possible?

Kristian Roth: I would say, once you have submitted your EUA, then you could definitely engage with your lead. But we prefer to have a submission on file in order to start that conversation.

Annie Wright: Oh, OK. OK. OK. Alright. But in the-- OK, so—

Timothy Stenzel: And I would add that, if your clinical study was pre-omicron, we do want to see omicron data, so include that in the submission, whatever you have.

Annie Wright: OK. Whatever we have-- OK, alright. Sounds good. Thank you so much.

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

Sarai Meyer: Hello. This is Sarai Meyer from Detect. This is a follow-up question with regard to the introductory announcements. It was mentioned that all molecular tests for point of care or laboratory use would fall under the 510(k) pathway based on BioFire. What about the case of a home use molecular test? Would that be able to use BioFire as predicate, or would it require a De Novo?

Timothy Stenzel: I think it's likely to require a De Novo, since we haven't authorized an OTC test. Kris, do you want to take this one?

Kristian Roth: Yeah. I'm a little bit hesitant to mention for sure that it's going to be a De Novo, because we would actually need to have-- to make that determination. But it's highly likely that a home test is going to be following the De Novo pathway. The risks are different. The benefits are different. It's a fairly obvious, I think, determination that we can say it ahead of time, but of course, we haven't made it official yet.

Sarai Meyer: Thank you.

Timothy Stenzel: Mm-hmm.

CDR Kimberly Piermatteo: Alright, thank you. Our next question is from Stacy. Stacy, I am unmuting your line. Please unmute yourself and ask your question.

Stacy Drakousis: Thank you so much. Good morning, and thanks again to the panel for hosting this forum. My question is surrounding the PHE, which was last signed on January 14. According to the declaration, it's good for 90 days, which brings us into April. Is there any indication presently that that is going to be extended again, or renewed?

Timothy Stenzel: Toby, you want to try to handle this one?

Toby Lowe: Yeah, I'm happy to. So this is what I was mentioning a little bit during one of the questions that came in by email. The issuance of EUA and the EUAs being in effect is based on a declaration by the Secretary of HHS that circumstances exist justifying the authorization of the emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19.

That declaration is different from the public health emergency that you're referring to. So the declaration by the secretary does not expire. It has to be proactively terminated. And as I mentioned before, the declarations-- the similar declarations for previous public health emergencies, such as Zika and Ebola, have not-- have still not been terminated.

So we do not have any information on the timeline of when the declaration that circumstances exist may be terminated, or on the 90-day public health emergency and whether or not that will be extended.

But we don't have any reason to believe right now that the secretary's declaration would be terminated any time soon. And we as you've likely seen with the transition guidance that I mentioned earlier, we are actively working towards getting information out and getting public comment on that transition plan.

Stacy Drakousis: Thank you.

CDR Kimberly Piermatteo: Thank you for that question. Our next question is coming from Heidi. Heidi, I am unmuting your line. Please unmute yourself and ask your question.

Heidi M.: Yes. Can you hear me?

CDR Kimberly Piermatteo: Yes, we can.

Heidi M.: OK. Sorry. The screen is gone. So I wanted to follow up on a previous question asked about usability and clinical studies, and their sequence and whatnot. I was wondering, would it be more sensible to conduct the usability validation prior to the clinical to ensure the safe and effective use before such, and then maybe potentially supplement and incorporate a usability survey with pointed questions when in the clinical to kind of demonstrate that the usability and comprehension of the device and the materials showed the same trend and success from the validation, and therefore supplementing that usability and safe and effective use statement of the device and materials carried through the clinical as well?

Timothy Stenzel: Yeah, so that's the traditional way of doing it, right —

Heidi M.: Right.

Timothy Stenzel: --to do usability first, and then the clinical study second if everything looks good in the usability. Otherwise, you can make changes to your instructions or device that address any of the potential usability concerns. What the FDA has done for this is to provide flexibility to compress timelines—

Heidi M.: Right.

Timothy Stenzel: --and shorten all of this down, and also potentially limit cost. But it does come with a risk, as I mentioned before.

Heidi M.: Right.

Timothy Stenzel: It could be unsafe in some way, and you have to stop the study. Or the usability test done at the same time, or essentially the same time, but after the clinical study testing and the session is done, that then you may spot something that needs to be changed, and you have to restart the clinical study too.

Heidi M.: Right.

Timothy Stenzel: We're just providing that flexibility. It's up to the developer to decide which path they want to take, the traditional or the shortened.

Heidi M.: Right. I guess, apologies-- I should have pointed the question more towards-- I've been seeing that there is a trend to incorporate usability surveys within the clinical, despite having already done validation. So I guess my question would be, is it-- in FDA's opinion, is it supportive to show that the usability perception of the user and performance in the clinical is kind of reflecting the same results of the usability study to show that, even-- because a lot of times there are changes, right?

And then there might be minor changes that don't require supplemental usability study per se. So would it be acceptable to kind of show that the usability and safe and effective use demonstrate it throughout the clinical with that survey, then, would that be considered supplemental data then?

Timothy Stenzel: Yeah, I understand that a little bit better. And that does seem logical. Kris, do you have any additional comments at this time? We're kind of getting into very specifics here, so—

Heidi M.: Right.

Timothy Stenzel: --it may require some dialogue directly between the FDA and the company.

Kristian Roth: Yeah, I would agree with that. What is exactly the design of your device? Is it similar to something else that's on the market or is it something you could put in the nude? Does that have an app? Is it visually read? I think there's a lot of variables.

Heidi M.: Right, right. Yeah. And I understand that that's very specific. I was just wondering if there is a general opinion that such data can be used as a supplemental data set to support a statement.

Kristian Roth: It's a possibility.

Heidi M.: Right. OK.

Kristian Roth: That's exactly what the situation is, I think.

Heidi M.: Yes. Thank you.

Kristian Roth: Thanks.

CDR Kimberly Piermatteo: Thank you, Heidi. 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 yourself? Alright, we are unable to hear you at this time. Please go ahead and raise your hand again, and hopefully we'll get back to you at a later time.

So our next question is going to come from Rakan. Rakan, I've unmuted your line. Please unmute yourself and ask your question.

Rakan Qazziha: Hello. Thank you for taking my question. This is Rakan Qazziha, Tracks Management Services CSO. I have a question regarding our clinical trial of OTC antigen kit. Our clinical director decided to change the comparator PCR kit because of the automated RNA extraction-- so just to prevent cross-contamination. And my question is, would it be-- is there anything that we should do, or is it possible, or is this allowed to do during a clinical trial? And should I even mention the name of the comparator just to make sure it will be acceptable on the list of the comparator PCR kits that you have for the molecular clinical trials?

Timothy Stenzel: Yeah, as far as names go, it's best if you send an email to our templates box and ask that. And then offline. So the other thing is I just want to clarify-- it sounded like you started your trial with one comparator, and then switched to another.

Rakan Qazziha: Sorry. Yeah, that's correct. We started with that—

Timothy Stenzel: OK.

Rakan Qazziha: Yeah.

Timothy Stenzel: What I'd do is I would provide that information in the email to the templates. You started your study with-- and specified the comparator, and then you switched the study after X number of patients to the next comparator. And just make sure that we think both comparators are OK. I don't know that there's automatically a problem using-- making the switch, but we would want to give you very specific feedback on that.

Rakan Qazziha: OK, great. Thank you. You answered my question.

CDR Kimberly Piermatteo: Thank you. Alright, we're going to try to get to two more questions today. Our next question is coming from Ho-Jun. Ho-Jun, I've unmuted your line. Please unmute yourself and ask your question.

Ho-Jun Suk: Thank you for taking my question. So my question is regarding the discrepancy analysis for the clinical evaluation for a molecular diagnostic test for point of care use. So I was wondering for the discrepancy analysis if it only has to involve the samples that are discrepant between the candidate test and the first comparator test, or the discrepancy analysis has to involve all the samples that were included in the initial evaluation with the first comparator test?

Timothy Stenzel: It depends. And it also depends on your original study design. It also depends on what you want to do. That's a very specific question for your situation, so I would recommend that you ask that in your submission-- or if you've already submitted, that you ask your assigned reviewer about that.

Ho-Jun Suk: Got it. Thank you.

CDR Kimberly Piermatteo: Alright, thank you. We're going to go back to Neda. Neda, I've unmuted your line. Please unmute yourself and ask your question.

Neda, are you able to unmute your line? Neda are you able to unmute your line.

Alright, with that, we will go and take one more question. We are going to hear from Sri Lekha. I have unmuted your line. Please unmute yourself.

Sri Lekha Eedulakanti: Hi. Can you hear me?

CDR Kimberly Piermatteo: Yes, we can.

Sri Lekha Eedulakanti: [INAUDIBLE] Laboratories. We have an antigen home test. Clinical study has already been completed, but we were only able to get four positive asymptomatic subjects. We have recruited over 75. We would like to know from the agency if we should be continuing that clinical study to supplement the EUA application that has already been with FDA now.

Timothy Stenzel: So it depends. Just to give some high level-- and if you were one to have submitted a question beforehand, we are planning on responding by-- in detail by email. But just as a reminder, we still have the serial testing pathway for asymptomatic. So as long as there's adequate performance on symptomatics-- at least 80% sensitivity to high sensitivity molecular test and a lower 95% confidence

lower bound of at least 70%-- you qualify for the serial testing claim for asymptomatics, with a post-market commitment to do an asymptomatic study.

If you don't have sufficient numbers of asymptomatics pre-market, and are seeking a single test asymptomatic screening, then that's not going to be sufficient for that claim. So just at a high level, that's what I can respond to today. But again, if you have or-- already asked this question specifically of our inbox, we're planning on responding to that in the next day or two. Or if you haven't and you need the details, then you can submit an email to our templates email.

Sri Lekha Eedulakanti: OK.

Timothy Stenzel: Thank you.

Sri Lekha Eedulakanti: Sure. Thank you.

CDR Kimberly Piermatteo: OK. Thank you. That was our last live question for today. I want to thank all of our panelists for providing responses to these questions. And we do appreciate everyone's participation.

As I mentioned earlier, a recording of today's Town Hall and a transcript will be made available on CDRH Learn. Please visit CDRH 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 our next IVD town hall scheduled for Wednesday, April 6, 2022. This concludes today's town hall. And have a great day.

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