Virtual Town Hall #80
March 9, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kimberly Piermatteo: Hello and welcome to virtual IVD Town Hall number 80 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.

I am Commander Kimberly Piermatteo of the United States Public Health Service. 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 moderating today's Town Hall.

A recording of today's Town Hall and 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 February 23rd IVD Town Hall recording and transcript have been posted.

The next scheduled IVD Town Hall will take place on Wednesday, March 23, 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, and Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices, also in OIR.

For today's Town Hall we'll begin with a few opening remarks from our panelists, followed by answering your previously emailed questions, and then proceed to answer your live questions.

I'd now like to welcome Tim, who will provide the first opening remarks. Tim, the floor is yours.

Timothy Stenzel: Thank you Kim, and welcome everyone. This is our 80th IVD Town Hall and we'll continue these series as long for COVID IVDs as long as there is a need and strong interest. Just wanted to let you know that. And we do have a lot of questions that were submitted ahead of time having to do with transition from EUAs to full authorizations, and Kris will go over those.

We are continuing to encourage submissions for full authorizations. We are accepting Pre-Subs, Q-Subs, regular Pre-Subs, Q-Subs, for them, and encourage them. And we want to do our part to help this transformation or this transition.

And so, with that I'm going to go into next a couple of web updates. So we did update the FDA's website and the links are in the PowerPoint and will obviously be available after the meeting too. And some of the website's updates are regarding serology, one of them is fairly straightforward and providing recommendations for traceability to an international standard. If someone is developing a quantitative test or wants to trace their semi-quants or other tests to international standard.

And then also we continue to get questions about whether or not SARS-CoV-2 antibody tests should be used to assess whether a person is protected from COVID, and the current FDA thinking is still that no, the current antibody tests should not be used for this purpose. We are still awaiting sufficient data to

establish thresholds for immunity and protection and should we have those, and when we have those, that will be a different situation entirely.

The other website update has to do with our COVID test basics web page. And this is largely focused on consumers. What is a diagnostic test? Was is a serology test? And how do you use them and what are they good for? So please check into those if you are interested.

OK, with that, I'll turn it over to Kris.

Kristian Roth: OK great. Thank you Tim.

I just want to highlight a couple of safety communications that recently that came out on March 1st. So these safety communications are CDRH warning folks not to use these tests, which have the same or similar names as FDA authorized tests.

I think the first we want to discuss is the Celltrion DiaTrust COVID-19 test. We are warning people not to use certain Celltrion USA, Inc. DiaTrust COVID-19 Ag rapid tests. People should not use this particular Celltrion test if it is in a green and white packaging.

The second test is the SD Biosensor Standard Q COVID-19 Ag home test. We are warning people not to use the SD Biosensor Standard Q COVID-19 Ag home test. This test is packaged in a white and magenta box and has not been authorized, cleared, or approved by the FDA for the distribution or use in the United States.

And the last one is a test from ACON Laboratories. We are warning people should not use the ACON Laboratories test named FlowFlex SARS-CoV-2 Antigen Rapid Test in parentheses Self-Testing, and this is packaged in a dark blue box.

For more information about these particular safety comms and what to be done if you come across these products, please go to these links and it's very thoroughly described within that text.

With that, I will turn it back over to Kim. Thank you.

CDR Kimberly Piermatteo: Thank you Tim and Kris for those opening remarks.

We'll now answer your previously emailed questions about COVID-19 Test Development and Validation. Please note we receive some questions that are too detailed or test case specific that we will not 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 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@fda.hhs.gov mailbox for an update.

Now let's get to the questions you sent in advance of today's Town Hall. Kris, I'll be directing these questions to you.

The first question is, would real-world data also be considered acceptable for subsequent marketing applications of other EUA products, such as molecular in-vitro diagnostic tests?

Kristian Roth: Yeah, Thanks Kim. We are open to considering existing data to support a regulatory submission if you believe that you have real-world data that can be used to establish performance of your test. We're glad to engage in a discussion to appropriately leverage that real-world use and experience as part of your marketing application.

CDR Kimberly Piermatteo: Thank you Kris. The next question we received is, will FDA prioritize De Novo and 510(k) submissions that were formally granted EUA, or will FDA review all serology submissions, including those for qualitative and semi-quantitative assays?

Kristian Roth: Yeah. Thank you. So I think there's two parts here. For the first part, FDA will review all MDUFA files that are submitted, and we're working hard to meet the established MDUFA timelines.

For the second part, we'd like to note that an international standard material for SARS-CoV-2 antibodies is available. Qualitative or quantitative tests should be considered in a manner similar to premarket submissions for other analytes which have international standard materials and that allow quantitative claims. These other examples are hepatitis and rubella.

CDR Kimberly Piermatteo: OK. Thank you. Our next question is, can FDA clarify whether a De Novo or 510(k) guidance document for serology tests will be issued prior to the announcement of EUA terminations?

Kristian Roth: Yeah, we can't comment on any future guidance or policy documents that may be in the works at this time or in draft, being drafted, however we will provide further details as additional information becomes available. Test developers interested in pursuing full marketing authorization for a serology test are encouraged to submit Pre-Submission to discuss your approach.

CDR Kimberly Piermatteo: Thank you, alright. The next question, is FDA currently reviewing any De Novo submissions for serology tests? If so, would it be possible to share recommendations provided to developers at this time?

Kristian Roth: So again, we're not going to comment on any submissions that may be under review, however if you intend to pursue a De Novo regulatory pathway for your serology test, we recommend that you submit a Pre-Submission with your study protocols, in order for FDA to provide appropriate feedback.

CDR Kimberly Piermatteo: All right our next question looks like it has two parts, so I'll read those two parts completely and then turn it over to you Kris for your responses. So the first part of this question is, for a De Novo or 510(k) serology test, would it be acceptable for the intended use to include monitoring of immune response to SARS-CoV-2 vaccination, or will claims be limited to use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2 infection? The second part of this question is, if testing of vaccinated individuals is not acceptable, would clinical studies of infected individuals require that vaccinated individuals be excluded?

Kristian Roth: Sure, thank you for that. Tim did discuss this a little bit at the intro and maybe I can add a little bit more in the context of this question. So currently, authorized SARS-CoV-2 antibody tests have only been authorized for use as an aid in identifying individuals with an adaptive immune response and have not been evaluated to assess the level of protection provided by an immune response to COVID-19 vaccination.

We have previously released safety communications stating that currently authorized SARS-CoV-2 antibody tests should not be used to evaluate a person's level of immunity or protection from COVID-19 at any time and especially after the person received a COVID-19 vaccination. While positive antibody test results can be used to help identify people who may have had a prior SARS-CoV-2 infection, more research is needed studying individuals who have received the COVID-19 vaccination.

FDA's feedback on EUAs, Pre-Submissions, De Novos, 510(k)s, have been consistent with the safety comm, and we continue to recommend that test developers do not include vaccinated individuals in their clinical evaluation.

CDR Kimberly Piermatteo: Thank you very much Kris. Alright, so our last pre-submitted question is, due to the recent decline in COVID-19 positivity rates, is it acceptable to test archive samples to supplement the positives tested during the clinical evaluation for an antigen point-of-care test?

Kristian Roth: Yes, thanks. So if pursuing an enrichment approach, which is really what this question is describing, you should appropriately tailor the study design for your specific test and you'll clearly document and describe how any bias associated with your proposal is minimized. We strongly recommend that you submit a pre-EUA with a detailed clinical study protocol prior to implementing any enrichment activities, such as using big samples.

CDR Kimberly Piermatteo: Great. Thank you Kris. That wraps up the previously submitted questions. We will now take your live questions. To ask a live question, please select the Raise Hand icon at the bottom of your screen. When you are called on, please identify yourself and ask your question promptly. Also please note, we are not able to discuss specific submissions under review.

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

Sam Ali: Yes, hello, hi, you hear me, OK?

CDR Kimberly Piermatteo: Yes we can.

Sam Ali: Alright great. So this is Sam at Intune.bio. The question is about self-testing usability studies. So we're running clinical trials for tests that are substantially similar to other tests that have been recently approved, and the question is how extensive are the usability study requirements for tests that have very similar workflow and process and interpretation of results, and even the instructions are primarily similar.

Timothy Stenzel: This is Tim and Kris may want to add something. So do check our current template for-- I think you're talking about an over-the-counter test--

Sam Ali: That's right, yeah.

Timothy Stenzel: --test at home, and probably antigen, I'm thinking, right?

Sam Ali: Yes, correct, yes. Yes, correct.

Timothy Stenzel: OK well take a look at the template, if you think that it's substantially equivalent to what we've authorized before, follow the template and then in your submission you can justify why you think that is the case. And you can at least reduce the user testing. I don't know the cost of this. It would vary depending on whether you do it yourself and how you do it yourself versus using some sort of external party. Kris, anything to add to my response?

Kristian Roth: No, thank you.

Sam Ali: OK, thank you. Thank you so much.

Timothy Stenzel: You're welcome.

CDR Kimberly Piermatteo: Thank you Tim. Our next question will be coming from Ron. I'm going to unmute your line, so please be sure to unmute yourself and ask your question.

Ron Domingo: Hello, can you hear me?

CDR Kimberly Piermatteo: Yes we can.

Ron Domingo: Alright. Thanks Tim and Kris. I have a client with a respiratory panel molecular diagnostic PCR based assay that includes COVID, flu A/B, and RSV, and they are currently conducting a clinical trial that started in February of this year. However, the prevalence of the viruses has dropped significantly since the December, January time frame. Even with prospective all comers collection it is likely that all of the category one samples will be negative. Would the agency comment on the acceptability to support an EUA as long as the required minimum number of positives outlined in the EUA template are achieved if the positive COVID samples are category 2 and flu and RSV positive samples are category 3, and what percentage of samples for the trial need to be category 1? Thank you.

Timothy Stenzel: Kris, you feel comfortable trying to respond to this question?

Kristian Roth: Sure. I think we all understand that certainly flu and RSV right now are particularly low in prevalence, and so I think we're open to different category sample types for those analytes. And you can look at some of the other decision summaries for multi-analyte EUAs that have been published and they describe sample types. I think the best and most accurate answer we can probably give you would be via email, and so really if you can kind of outline the difficulty that you're having, I'm sure we can come to a path forward. This is not the first time that we've encountered this and I think we do have a couple of ideas of what's acceptable and likely to be a balance between what you can provide pre-authorization and post-authorization.

Timothy Stenzel: And Kris, anything specific about COVID, about SARS-CoV-2?

Kristian Roth: For COVID, yeah. Taking archive samples is completely acceptable for the suspected population. If you're looking for a screening claim, that may be a little bit different but certainly for that suspected population archive samples are perfectly fine.

Ron Domingo: Hello.

Timothy Stenzel: All right. Ron is that you?

Ron Domingo: Yeah, just as a follow up, you asked me to send an email. Could I highlight on the subject Tim and Kris?

Kristian Roth: Sure. Please do.

Ron Domingo: OK thank you very much.

CDR Kimberly Piermatteo: OK. Thank you Ron.

Ron Domingo: Sure.

CDR Kimberly Piermatteo: We're going to go ahead. Our next question is from Sue. Sue, I'm unmuting you now. Please unmute yourself and ask your question.

Sue Hart: OK my name is Sue Hart from Hemex Health and I have two questions, if that's OK. I'm wondering if, this is for antigen POC, if an investigational use device that you're putting into a clinical study can be used at a site that doesn't have a CLIA waiver?

Timothy Stenzel: So that's not necessarily what we're recommending here because we're trying to look at performance within an actual CLIA site. And with the kind of personnel that you see at a CLIA site, presumably a busy clinical practice, where the staff there are juggling seeing patients, taking care of those patients, and doing any CLIA waived tests and that that's the scenario that we're trying to-- that we're recommending.

So that we know, in that busy environment, can they get an accurate test result? And I'll allow a follow up question there. But that has been our recommendation for a long time now.

Sue Hart: OK because we've got a POC site that is doing-- its a drive-through PCR site, PCR test site. But they don't have a CLIA waiver because they're doing the PCR testing at their laboratory that is a few miles away.

Timothy Stenzel: Say that again. You're doing the candidate device testing at a drive-thru setting.

Sue Hart: Yeah because we're rapid and they do the collection of the PCR swabs at the drive-thru site and it's pretty busy, but the lab for PCR testing itself is a few miles away so they bring the swabs there.

Timothy Stenzel: Yeah so the comparator testing, that's pretty standard that you'd have to transport that somewhere else. Again we're looking for a standard POC site so, Kris, you may be able to add on to this, but I think if you're going to have multiple sites and one of those sites is such a site that's fine. But the drive-thru site should have, first of all should have a CLIA certificate if they're doing CLIA lab testing.

So unless they're doing just collection and sending to a central facility but if it's going to be a nonstandard point-of-care testing site that you want to use, or at least one site that you want to use, I would recommend you submit a pre-EUA that includes your clinical study design and your method for testing, and verify with the FDA that that's acceptable.

Sue Hart: OK the second question has to do with an OTC submittal and antigen submittal. If you also want a POC claim, do you need a study, an additional study, that includes the intended POC user and that environment?

Timothy Stenzel: No. So we'd recommended a long time ago that those that are ultimately interested in going over-the-counter, they just do the over-the-counter studies. They don't have to do-- there are all the flex studies but they don't have to do-- we don't recommend doing clinical studies within a point-of-care if you're going to do the home user study. If something works well in home user hands, we expect to work well in point-of-care user hands. And that just comes with it, you don't necessarily have to have a point-of-care version of the test but you can have a professional use of the test and you don't need any additional clinical study data to support the point-of-care in that case.

Sue Hart: OK, alright. And in that case, in your intended use, do you not say CLIA waived for that environment? You just say point-of-care environment?

Timothy Stenzel: So it depends on you and what you want and typically a professional use kit is going to have a lot more tests than an over-to-counter kit, so you would, in all likelihood, have two separate authorizations with one submission.

Sue Hart: Yeah, OK.

Timothy Stenzel: We would assign a second EUA number for the point-of-care kit, you would have different kit sizes, their labeling would be a little bit different, how you describe the setting where it happened. And then on the FDA website for a successful test, you will have both over-the-counter designation on the website, as well as CLIA waived, moderate and high complexity settings.

Sue Hart: OK so would you submit two sets of labels in that case also?

Timothy Stenzel: Yes.

Sue Hart: OK.

Timothy Stenzel: Yes.

Sue Hart: Thank you. Oh that's awesome.

Timothy Stenzel: You're welcome.

Sue Hart: Thank you.

CDR Kimberly Piermatteo: Thank you, Sue. Thank you, Tim. Our next question comes from Ray. Ray, I'm going to unmute your line. Please unmute yourself and ask your question.

Ray Bandziulis: Hello, thank you for taking the question. My name is Ray Bandziulis from LGC Biosearch Technologies. This question is in the category of additional conditions of authorization that FDA issued related to-- for molecular tests that were already authorized related to the monitoring of variants. And for the request, the conditional authorization was for manufacturers to submit reports on how their monitoring programs were structured, as well as some labeling modifications to the existing materials.

In the case of LGC, those materials were due December 21st. Does FDA still intend to provide feedback on the manufacturer's program? And related to that, in the absence of feedback, should manufacturers continue to provide regular updates on the program even if prevalence is not detected at or above 5% occurrence? Thank you.

Timothy Stenzel: So yeah, you're welcome. So we've got a guidance out there and we've also updated the authorizations as you mentioned. I think this-- Kris, if you want to handle this, it'd be an excellent one for you to handle.

Kristian Roth: Yeah so we do have a rather large backlog of these particular files, so you may have not heard back from the review team yet on your supplement. I think we really only are interested if you detect changes in reactivity. If you continue to monitor the publicly available databases and there's no change, there's no reason to report. We will of course, be doing the same thing on our side and if there is some changes that we detect, we will likely reach out to you as well. So I would just say, keep doing your typical monitoring that you are doing and if there's no signal that things are changing then certainly we want to keep those reporting activities at a minimum.

Ray Bandziulis: Great, thank you.

CDR Kimberly Piermatteo: Alright thank you. Our next question is coming from Tracy. Tracy, I'm unmuting you now. Please unmute yourself and ask your question.

Tracy: Hello doctors. My name is Tracy, Tracilynn Kidd, they call me Tracy. I'm independent quality consultant, and I had a question about the submissions on the clinical testing kits or systems for submission for emergency use authorization. How is the validation approach for determining the shelf life where the expiration date is being monitored?

Timothy Stenzel: So there's different expiration dating experiments that can be done. I think our templates that are on the FDA website speak to some of these.

You really want to start with the target date for your unopened kits at least for ultimately where you want your expiration dating to be. Let's just say you want it to be two years for molecular and/or rapid antigen tests or a serology test, then you plan your expiration dating experiments out beyond that date. You want to go one time point beyond those dates. And then there's been a lot of interest to seeing date extension for expiration dating for COVID tests, so that especially when there's drop off in cases, perhaps only temporarily, product doesn't go bad in the intervening period, and labs have stocks and individuals that have stocks of tests.

So we are encouraging that all developers extend their dates. And so in the early months you may want to have more time points. Once you get up to say one year, you may want to go quarterly in real time work up to a year, and then you might drop off to every six months or something. That's up to the sponsor.

But we like to see real time-- we'd like to see accelerated stability testing for the submissions so that we know that we can give at least six months dating at additional authorization. And then as you do your real-time stability testing and have updates, those are supplements and submissions. The FDA reviews the data and if it looks good, can authorize it.

And then also we've displayed extreme flexibility for kits that are already in the field, that may be expiring because they have an earlier expiration date or a shorter expiration date than has just been authorized. And so we do work closely with firms to address that issue. So that kits in the field with FDA authorization can be used beyond the original dating with information provided by the developer. I'm not sure if that addresses all your questions. I mean, to get into a detail response on how to do that would be too much for this call. Do look at the templates and then if you have questions beyond that you can submit those as part of a pre-EUA.

Tracy: Great thank you, and thank you Kimberly.

CDR Kimberly Piermatteo: Thank you. Our next question is from Murthy. Murthy I am unmuting your line. Please unmute yourself and ask your question.

Murthy Talasila: Hi, can you guys hear me?

CDR Kimberly Piermatteo: Yes, we can.

Murthy Talasila: Thank you. My question is around the EUA timeline as we try and plan for our market approach. So I don't think any of you would be talking about our specific case submission, but I'd like to understand what is a typical timeline once we're in an active review process?

Timothy Stenzel: So that's typically not information that we give out. We're still receiving upwards of about 100 original EUAs and pre-EUAs a month, so we remain very busy. The surge has largely returned to their original spots within the Center, but we have been able to hire very well through the pandemic with additional funding provided by Congress. So the DMD Division, the Microbiology Division, is substantially larger than it was pre-pandemic.

And so we do have our priorities that were listed at the November 15, 2021 guidance update. You can see what those priorities are. If you meet those priorities and your submission is excellent, meaning that the data support the test authorization and the data is presented in a way that's easily understood and complete and all the protocols are provided, that you used, and they're able to be understood, those submissions go through very quickly. Sometimes very quickly, even now. However if we have questions, that can involve a lot of back and forth. And that's going to extend. So those submissions that are well done in all aspects really benefit from that focus to making sure that it's a well-done submission.

Murthy Talasila: OK thank you.

CDR Kimberly Piermatteo: Alright our next question is coming from Jennifer. Jennifer, I'm unmuting you now. Please unmute yourself and ask your question.

Jennifer Stanford: Hi, this is Jennifer Stanford from Hopkins Med Tech Compliance, and my question is regarding over-the-counter rapid antigen tests. We have been using NP swabs as our standard of care for PCR testing, and on other calls we've talked about the potential of switching to anterior nasal swabs. So if we did an anterior nasal swab for our PCR, and then we also did an anterior nasal swab for the over-the-counter test, would you all want to see a randomization between those two types of swabs?

Timothy Stenzel: OK so this is a clinical study protocol where you have a candidate antigen tests.

Jennifer Stanford: Yes.

Timothy Stenzel: And Kris may want to answer, add some additional to this. So first of all, the sample type for the comparator test has to be authorized. It has to be an EUA-authorized test to be used as a comparator and we want it, we recommend it to be a high sensitivity. So we are recommending that the developers do check with the FDA to make sure that the particular molecular comparator test is of sufficient sensitivity for your study. That's a pretty easy direct question if you're not going to have any other questions that can probably be handled by an email rather than a pre-EUA.

And then if the antigen test, if you want to go with an anterior nasal swab, then as long as the anterior nasal swab is acceptable and validated and authorized for the molecular comparator, comparing the two is just fine. It may be clear to you already but sometimes it's not clear. And then there are different approaches to this as far as you can-- oh randomize, this is an OTC test, so we don't like to have the users biased, at least immediately biased. I mean most everybody has had some sort of swab done on them but sometimes they forget. And we're really evaluating, for an OTC test, you know how does that user approach that test with just the instructions that are provided with the test without any help. And so the comparator test of swabbing could give them a little bit of education right before they do the antigen test.

So the best situation here that we recommend, if you want to do something other than this, then I would recommend that you submit a pre-EUA with your clinical study design. There may be other questions you have. Is to first give the candidate test to the subject, and have them do that, and then have a short washout period of, we would recommend 15 minutes, and then you come back with the comparator test. So since most of these tests, if the user goes ahead self-swabs, runs the test, it's going to be at least 15 minutes already. So it's really as soon as they're done performing that OTC antigen test, you can then direct them into getting their comparator test swab done.

Jennifer Stanford: OK. Thank you.

CDR Kimberly Piermatteo: Alright thank you very much. It looks like we're going to receive another question from Sam. Sam I'm going unmute your line and you can ask your question.

Sam Ali: Yes, this is Sam again from Intune.bio. Thank you for taking my second question. This is a follow-up question to something that was mentioned last time at the last Town Hall, about enrichment in clinical trials. As you know, the numbers, the number of cases are going down, and for, again the question is for OTC self-testing antigen tests, can you give us maybe an example-- I think Kristian mentioned the enrichment last time, but it was a bit vague, but is there an example of an acceptable enrichment approach for antigen tests?

Timothy Stenzel: Yeah so a lot of this has to be individualized because there's specifics that are important. What we want to do is eliminate bias, and enhancing the performance of the test through that bias, so since this is an over-the-counter antigen test it's really important that the user doesn't know the results of-- it's important that they don't know whether they're positive or negative with the test of record or comparator test.

So first of all, antigen tests are directed at symptomatic people, so obviously someone has symptoms and can define those symptoms, that can help you enrich. If there's a way that you can have a quick-- I

think it's probably good for you to come in with a pre-EUA and suggest some things. But those are the important elements, and it all depends on what the comparator test is, how quickly you can, or the test of record, if it's the same thing, as compared to how quickly you know that result, and then what's ethical and when you provide that result to the user, relative to when they are tested. One possibility is, if the local IRB would approve, is that you bring people back to give them their results of their testing. If they, at the time of the original testing, say they're willing to be part of a study, and you bring back both people who tested positive on the test of record, as well as tested negative so there isn't a bias there.

And so they don't know whether they were positive with the comparator test or not. But that's just one idea, it's not necessarily the recommended approach, it's just to get your creativity going here on how you might do it and to lay out the importance of avoiding bias.

Sam Ali: Yes. Yes, I understand. Thank you so much.

Timothy Stenzel: Mm-hmm.

CDR Kimberly Piermatteo: Alright our next question is coming from Zakir. Zakir, I am unmuting your line now. Please unmute yourself and ask your question.

Zakir Murtaza: Hello, good morning. Yeah, this is Zakir Murtaza from Applied Biomedical. I have a question regarding cross-reactivity to be recommending it, we have to have an organism, inactivated organism but some of them are not available. Is there any recommendation where we can acquire those kind of samples?

Timothy Stenzel: So I think you're talking about cross-reactivity testing.

Zakir Murtaza: Right, yes.

Timothy Stenzel: ---that can be done wet. Some can be cultured and some can't. And the type of tests that you're developing is, I presume an antigen test, then?

Zakir Murtaza: Antigen test, yes.

Timothy Stenzel: Yeah, so it's a little bit more difficult to do *in silico* analysis. I'm not going to say it's impossible, but you know I'm not sure that science is there yet. So that's the sort of thing that you could ans--

Zakir Murtaza: We are using recombinant but not all of them are available. So some of them are available. So we are planning to do that, but some of them recombinant proteins are available. So that's what we are planning to do unless we find some real organisms.

Timothy Stenzel: Yeah. Yeah, so I think we have a pretty standard list that we know are available.

Zakir Murtaza: Yeah.

Timothy Stenzel: And then those that aren't available, I don't know that I'm up to speed on the use of recombinant for those. Kris, are you?

Kristian Roth: Yeah, I don't think we've accepted recombinant quite yet. EEI has quite a few clinical lab collaborators that you can engage with. There are other sample banks that provide samples as well. So you can always [INTERPOSING VOICES] just and always discuss your due diligence with us and say, well hey we looked and we can, in some cases we can point you in other directions.

Zakir Murtaza: OK, very good. Thank you.

Timothy Stenzel: Yeah so, I was just going to recommend that you write you write up your cross-reactivity study protocol and the suggestions that you want to do and the rationale, you send that in as a pre-EUA for us to review.

Zakir Murtaza: OK. Thank you.

Timothy Stenzel: Thank you.

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

Wen Li: OK thank you, can you hear me?

CDR Kimberly Piermatteo: Yes we can.

Wen Li: Yeah thank you. Yeah, I'm Wen Li Zhou from XYZ Laboratory, and I just have a question on when we do the analytical performance for the antigen OTC kits and from the antigen template. We use this spike in the quantified virus inactivated. So right now, for the EUA application we have all been using this, the commercially available from ATCC and such other places. And to do this study, and recently there's a WHO standard that come out, so I just wondering for the De Novo or 510(k) are you expecting us to use this WHO standard for that or we still use the same way as the EUA studies?

Timothy Stenzel: No. This is for an antigen test or is this for a molecular?

Wen Li: Antigen. Antigen.

Timothy Stenzel: Yeah, so I don't think we would be recommending that you use WHO standard unless, a WHO standard, unless you were interested in developing something that you wanted to link to international standard units. Rather, following the existing templates and obtain inactivated virus that's been in use and do and do your studies with that. Kris, anything different than that from you?

Kristian Roth: No. In fact, WHO doesn't recommend use of their material in that manner anyways. They are providing that primary standard to folks that they're making a secondary standard and then using that secondary standard for further investigation. So really that primary standard for WHO really should be used according to instructions that WHO provides.

Timothy Stenzel: Yeah. So they don't have an under limited amount of international standards. So we don't recommend that be used for other than the intended purposes for that standard.

Wen Li: OK. Great, thank you.

CDR Kimberly Piermatteo: Thank you. Our next question is coming from D. Rafferty. I have unmuted your line. Please unmute yourself and ask your question.

D. Rafferty: Hi. Good afternoon. Thank you for taking my question. In reference to previous Town Hall meetings, on February 9th we actually heard information about the sequencing of at least 10 positive samples. And in regards to that, if it comes for the OTC or the POC antigen test, can the-- because currently the lab where we currently work in, they unfortunately they don't do sequencing, and we were wondering if these sequencing samples, even if they are collected in the United States, if they can be processed outside the United States. And I have another question, but I would like to hear the panel's opinion for that.

Timothy Stenzel: Is the study being conducted in the United States?

D. Rafferty: Yes, sir.

Timothy Stenzel: Mm-hmm OK, well there should be plenty of opportunities to get a sequence within the United States. We do ask that it's been a well-validated method of sequence analysis. And then as long as you collect, as long as the study is conducted when omicron is essentially 100%, which it still is, in a region of the country or world where you, well in this case, the country recommended, then we don't need to see the sequence information at the submission. That can be verified later. So we don't want to hold up the submission unnecessarily if the sequence information isn't back, as long as you've collected the samples. If you haven't even started your study and you start your study now, it's mostly going to be omicron. We just want to verify that at least 10 of those pre-authorization are omicron. And then again that sequence information can be submitted as soon as you can get it if it's not quite ready when you submit your file.

D. Rafferty: Thank you so much, Dr. Stenzel. And second question, if I may ask, can the accelerated study or the real time study for the stability, can part of it be supplemented with a study done and performed outside the United States, while we continue performing our tests within the United States?

Timothy Stenzel: Yeah, so if you've launched your test outside of the United States and the test is unchanged from what you're using, what you're going to submit to the United States, then that information can be applied to the current test as long as there's no changes to the test.

D. Rafferty: Great, excellent. Thank you so much for your time.

Timothy Stenzel: Mm-hmm.

CDR Kimberly Piermatteo: Thank you. Our next question will be from Nancy. Nancy I'm unmuting your line now. Please unmute yourself and ask your question.

Nancy Rector: Hi, thanks I'm Nancy Rector from Recuro Health. I have a real quick question about EUA templates. Is there one that is specific for the submission of digital test data for digital interpretation of over-the-counter rapid test results?

Timothy Stenzel: Digital test interpretation for over-the-counter tests?

Nancy Rector: Yeah, test results.

Timothy Stenzel: Yeah, so you mean that, say a smartphone would capture an image and call the result as either positive or negative--

Nancy Rector: Yes

Timothy Stenzel: or failed, or--?

Nancy Rector: Yes exactly.

Timothy Stenzel: And do we have recommendations? So I don't know how extensive the recommendations currently are in the template, but there is some direction there, I know. And then we do have a team that's focused on the review of those digital submissions, and they're pretty up to speed. So if you want to think about what-- if it's smartphone based, versus you have an instrument that does it right, that's dedicated for your test, if you want to use smartphones they've got to figure out which smartphones are going to be allowed to be used with the test, then have a validation plan for those different smartphones and also take into account different models within that family of smartphones. So if you want to go ahead and put together a protocol for validation of that and submit that as a pre-EUA that digital team can provide some feedback to you.

Nancy Rector: Great, thanks. We've been taking photos for a while, so we just are looking how to move forward. So thank you so much for all that you all do, for sure, and you've answered my question. Thanks.

Timothy Stenzel: OK thank you.

CDR Kimberly Piermatteo: Thank you Tim. We will try to get in two more questions. Our next question is going to be from William. William, I have unmuted your line. Please unmute yourself and ask your question.

William W.: How are you doing? My name's William from Texas, and my background is procurement and quality control. So, quick question, will Chinese-made OTC antigen tests be on the priority test?

Timothy Stenzel: National origin doesn't determine our priority. Our priority is listed on our guidance update on November 15, 2021, established what the priorities are. Many of the recent authorizations have been outside the US, have been manufactured outside the US.

William W.: Thank you, that's it. I really appreciate the answers.

CDR Kimberly Piermatteo: Thank you, William. Thank you, Tim. Alright we will move on to our last live question for today. That will be from Sousan. Sousan I am unmuting your line. Please unmute yourself and ask your question.

Sousan Sheldon: Hello, this is Sousan Sheldon. I'm an independent consultant. Thank you Tim and Kris for doing all you do, and the rest of the team at OIVD.

I have a question regarding the usability study for over-the-counter test that's going to be done in the US. Is it sufficient to have the final instruction for use for the patients to go through the testing and then

give them the 15 minutes, washout and sample the one for the comparator test and the study would be just that. Otherwise, I have thought about adding a questionnaire to the study protocol where the patients respond about the ease of the test, how difficult it was, and things like that to be able to tweak the instruction for use after the study. And if that happens, do I need to redo another usability study?

Timothy Stenzel: Yeah, so first of all, collection of the comparator test you can do exactly as you described. I think I mentioned that earlier on this call. Where you give them the kit and current instructions and they run the test without help, and then as soon as they're done obviously you can collect a competitor sample and not bias that.

If you don't think you have locked down instructions in your usability study creates questions about whether you should change your instruction. I mean that's really, could be material. And so its why traditionally, people do usability studies ahead of the clinical study. Because if they make any changes there's no impact on the clinical study.

If developers have high confidence there doesn't need to be a change that they have their protocol and their test locked down, it's going to perform well, then there's probably low risk and you save a lot of time if you combine things. But if you really want to know, is the test easy to use and will it, with the current instructions work, it may be best to do the usability study ahead of the clinical study.

Sousan Sheldon: Great, thank you so [INAUDIBLE] that's very helpful.

Timothy Stenzel: Yep. You're welcome.

CDR Kimberly Piermatteo: Alright. Thank you Tim. That was our last live question for today. And thank you to all of our panelists for providing responses to these questions. We greatly 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 the next IVD Town Hall scheduled for Wednesday March 23, 2022. Thank you. This concludes today's Town Hall and have a nice day.

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