Virtual Town Hall #79
February 23, 2022

Moderator: Joseph Tartal

Joseph Tartal: Hello and thank you for joining us today. I am Joseph Tartal, Deputy Director in the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. And I'll be moderating today's program.

Welcome to Virtual IVD Town Hall Number 79 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in response to COVID-19. Today's presentation and transcript will be made available at CDRH Learn under the subsection title Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. The January 26 and February 9 town hall recordings and transcripts are posted. The next scheduled IVD town hall will take place on Wednesday, March 9, 2022.

Our panelists for today's program are Toby Lowe, Associate Director for Regulatory Programs in 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.

We'll begin today's program with opening remarks from our panelists. And they'll provide updates and answer your previously emailed questions about COVID test development and validation. Please note we received some email questions that are too detailed or test case-specific that we will not address on the call. For those questions, we'll try to send a response in writing within a few days. If you have submitted a question and do not hear it addressed, please look for a written response. If you do not receive one within a few days, please feel free to reach back out to CDRH-EUA-Templates@fda.hhs.gov mailbox for an update.

And then last, we'll open with your live questions. So now I'll hand over to the program to Toby for opening remarks and updates. Welcome, Toby.

Toby Lowe: Thanks, Joe. Thanks everyone for joining us again this week. So we only have one update today and that is that yesterday we posted a new web page that lists the over the counter, at-home COVID-19 diagnostic tests.

We had had quite a few requests for a more consumer-friendly, user-friendly version of that list since the EUA tables include quite a bit more information and much more technical information. So we did just get this out yesterday with a more consumer-facing page there for the home tests.

And then beyond that, we can jump right into the questions that we received ahead of time.

Joseph Tartal: OK, thank you Toby. We'll start with those emailed questions. So the first question I have for you is, with the development of multiplex tests that can detect a combination of viruses, for example SARS-CoV-19 and influenza, is FDA in a position to consider an emergency use authorization for these combination tests at this time?

Toby Lowe: Yes. FDA has authorized several molecular and antigen multi-analyte diagnostic tests intended for use at laboratory and point-of-care sites. And the first two tests that we've granted full

marketing authorization to through De Novo and then a subsequent 510(k) are also multi-analyte respiratory panels. Those are both from BioFire.

At this point, we do not have any multi-analyte, over-the-counter tests. But we are willing to consider this. And we've noted previously on this call that if you're considering an over the counter, multi-analyte test, we recommend that you submit a pre-EUA to discuss your test design and proposal.

Joseph Tartal: OK, thank you, Toby, for that comprehensive answer. And our next question, are test developers of new over-the-counter antigen tests required to provide sequencing data for all positive samples after January 15, 2022?

Toby Lowe: Yes. We've discussed this previously on the call as well. And Tim has given fairly comprehensive discussion around this area.

We do expect that you provide sequencing data on all positive clinical samples for antigen test EUA requests. If you already have a submission in house and don't have that information, we would encourage you to reach out to your lead reviewer to discuss the best approach there. And if you are working on submitting a new EUA request, we do request that you include that sequencing data in your submission.

Joseph Tartal: OK, thank you. And for our next question, for an over-the-counter antigen home test clinical study, should we sequence only the samples that are positive on both the RT-PCR molecular comparator test and the antigen test, the subject test?

Toby Lowe: No, we would expect all positive samples, whether positive on RT-PCR, antigen, or both, to be sequenced for an EUA request for an antigen test.

Joseph Tartal: And going to our next question, can FDA clarify how test developers should address the low prevalence rates and an increase in weak positives during an antigen clinical validation?

Toby Lowe: There are multiple options for clinical study enrichment. And those approaches should be tailored to your specific test and the claims that you're validating. So we are recommending that developers submit a pre-EUA to discuss possible enrichment approaches. And then during that review of the pre-EUA, we can discuss alternate study designs that would streamline the enrollment of positive subjects when the prevalence drops very low or other strategies to increase the likelihood of detecting infected individuals.

Joseph Tartal: OK, and our next question, given the low prevalence of flu rates in the country right now, what clinical validation strategies would FDA recommend to support authorization of a multi-analyte test?

Toby Lowe: So we have discussed this on this call previously as well. And we do continue to recommend using a perfective clinical study to evaluate the clinical performance of your COVID-flu combined test. And we would recommend that you conduct that study for at least two weeks. And after the two-week duration, if you're not able to collect the recommended number of positive flu specimens, you can then proceed with a clinical validation study using banked samples at one of your testing sites.

And if you do that, we recommend that you test archived positive and negative clinical samples. And we do recognize that there was a reduced prevalence of influenza last season and that archived specimens may be difficult to obtain. But that is still our current recommendation to support authorization. And you can come in and discuss that with us if you're having trouble reaching those recommended numbers.

And then generally we would also consider adding a post-authorization commitment for a clinical study. And we would discuss that with you during the review of your EUA. And I can also note that there's additional information in the EUA templates on this topic.

Joseph Tartal: Thank you, Toby. And this is our last email question of the town hall. Can we use nasal swabs that are not listed in the 510(k) premarket notification database? And how do we ensure that swabs are legally marketed even if sourced from a third party, such as a distributor?

Toby Lowe: Yeah, so swabs typically are 510(k)-exempt devices, which means that they don't generally require premarket review. So they're considered to be legally marketed if they comply with other regulatory requirements, including registration and listing. So the FDA registration and listing database includes all device manufacturers and devices that are registered and listed.

And so you can search that database for the specific swab manufacturer and specific swabs that you're looking at. So typically, swabs that are used for upper respiratory collection should be sterile. And so the requirements for the sterile swabs do include manufacturing under 21 CFR 820, which is the quality system regulation for medical devices.

And then there are some swabs including those that are provided with viral transport media that are not exempt from premarket review. And so those swabs will be listed in the 510(k) database once they're cleared.

And in terms of purchasing from third parties and distributors, that is certainly acceptable. Swabs can be purchased from third parties or distributors as long as they are also following the pertinent regulations that apply to them.

And for any medical device including swabs, the outer packaging must include information that's noted in the labeling regulations. This would include the manufacturer and product name along with other information that's noted in that regulation. And then as I mentioned before, you can look in the registration and listing database to make sure that swab is listed there. And if it's not listed in the registration and listing database, then it may not be a legally marketed swab. And you should consider switching to one to a swab that is legally marketed to acquire a patient sample since you should be using sterile and appropriately marketed swabs for collection of patient samples.

Joseph Tartal: Thank you, Toby. And that's the last of our emailed questions. So next, we're going to get to the live portion.

So now let's take some live questions from you. Remember, to ask a live question, please select the Raise Hand icon at the bottom of your screen. When you're called on, please identify yourself and ask your question promptly.

Also, please note just like with the emailed questions we're not able to discuss specific submissions that are under review. So there may be times where we'll ask you to email that question to the templates mailbox because it's a very specific type of question.

With that, we're going to take our first live question of the day. So Thomas, please unmute yourself and ask your question.

Thomas Soriano: Hi, Toby. This is Tom Soriano from Diagnostic Oncology calling. I wanted to clarify something that seems to be different from what Tim and you have been saying over the past several months. And that goes to the sequence that we would collect, the comparator swab versus the investigational swab. And this is for a rapid molecular test.

So the way I understood it over the past several months was that you guys wanted us to collect the comparator method swab first and then run the investigational, take the investigational specimen and then run the investigational test right there. One of our customers got feedback from a reviewer that stated the opposite. So could you please clarify for us?

Toby Lowe: Yeah, thanks for that question. I can get this started, and then I'll see if Kris wants to add anything. So generally, the recommendation to collect the comparator swab first is generally specific to if you're using the comparator also for treatment. If it's being used for standard of care, then that should be taken into consideration.

But the template does discuss that the order should be randomized in your clinical evaluation. So we would want to see that generally that the order is random so that there's not a preference given to one or the other of the tests being performed.

Kris, do you want to add anything there?

Kristian Roth: No. Well, yes, I suppose. Randomization I think is a path forward especially for some instances where, as Toby mentioned, that first and the comparator method is not being used for standard of care. So allowing folks to do that, take a randomized approach, you know maybe it allows some flexibility in a trial if you're executing something at home or in some setting in which it's more difficult to ensure that one is taken first or second.

So it's just something you could discuss with your lead reviewer. You could send it to templates email box. But it is something that again, as Toby mentioned, it is in the—

Thomas Soriano: So this device is going to be intended for over the counter. And that's why we're particularly concerned about the sequencing issue because if we-- just as you said, Kristian there may be-- in order to not proctor the subject doing the test, it almost becomes an issue where it would be wiser to have the comparator taken when the subject shows up at the site and before they get started with actually doing the investigational procedures.

Kristian Roth: And that's fine as well. And then I think in that case, we recommend what we call a washout period or something to ensure that there is sufficient time for that mucosa to regenerate.

Thomas Soriano: Yeah, OK. Thanks, guys. I appreciate it.

Joseph Tartal: Thank you, Thomas. Our next question is from Veronica, Veronica unmuting. Please unmute yourself and ask your question.

Veronica Colinayo: Hi, this is Veronica Colinayo from Beckman Coulter. Yesterday at the webinar for the COVID-19 transition policy for devices, there was mention of possible review prioritization of De Novo or 510(k) submissions. I'd like to understand if FDA will be reviewing all serology submissions, including those for qualitative or semi-quantitative assays. Or will they be practicing similar prioritization that's currently being implemented for EUA?

Toby Lowe: Thanks for that question. The transition guidances that were put out and that were discussed in the webinar yesterday were put out for comment. And so we do recommend that if there are points that are unclear there that you submit comments to the docket.

And we can't really comment fully on what will or will not be done at that stage since that guidance is out in draft for comments and not for implementation. So the prioritization that we've laid out in our current COVID test policy guidance still holds for our EUA requests. And that does provide our current thinking about the priorities that are important for the current public health needs.

So that is something that would be considered as time goes on. Right now we have specified that quantitative is where we're prioritizing given the WHO standard that's available. And so we will continue to consider what those priorities should be.

Veronica Colinayo: Thank you.

Joseph Tartal: Thank you. Our next question is Karl. Karl, I'm going to unmute you. Please unmute yourself and ask your question.

Karl Enters: Hey, Toby. It's Karl Enters from GENETWORx. I expect we get a lot of questions after the webinar yesterday. And so everybody's thinking about timing now after this webinar yesterday.

And so for those of us who are seeing our LDTs to EUA two-week notices that we haven't even gotten a reviewer yet. And many of us are thinking of filing new EUAs. What kind of priority review can we expect on a new EUA filing? Or at least what does that time frame look like in the review cycle?

Toby Lowe: Sure. So if you are receiving two-week notices but you haven't gotten a reviewer yet, that generally indicates that you are sort of in the queue but may not be top priority for a review, if you will. And each EUA request that comes in, we do an initial triage review to determine if there are any glaring public health concerns with the submission, in which case we would-- if it's a test that's already being offered, which isn't typically the case anymore since all of those should already be in house given the updated November 15 policy.

But also, we look at whether there's a high potential impact on public health if it's a priority submission. And we do prioritize those for review regardless of whether there are other submissions that are sitting in the queue. And so it's hard to give a firm answer on the timeline for an EUA request, even for a new EUA request. We do recommend that you consider the priorities that are included in the policy. And submissions that include priority tests and that include complete information are generally going to get through review faster.

Karl Enters: Thanks so much. That was helpful.

Joseph Tartal: Let's go on to our next question. Our next question is from Erika. Erika, I'm opening up your microphone. Please unmute yourself and ask your question.

Erika Bladholm: Hi, this is Erika Bladholm from Beckman Coulter. I'm wondering, will De Novo or 510(k) guidance documents for serology tests be issued prior to the announcement of the EUA terminations? Will those guidances include the intended use of these assays for naturally infected patients as it is now, or will it also include vaccinated patients?

Toby Lowe: And that's a great question. Unfortunately, I'm not going to be able to answer it. As I'm sure you're familiar, we generally can't discuss policies that may be in the works. And so we don't have any previews of De Novos or 510(k) guidances that may come at some future point or any timeline on that.

Erika Bladholm: OK, thank you.

Joseph Tartal: Our next question is from Sarah. Sarah, I'm unmuting your mic. Unmute yourself, and please ask your question.

c Yes, good afternoon. My name is Sarah Helber also from GENETWORx. My question is given that the FDA has accepted CLIA-compliant data for the EUAs to date, will that data be acceptable in the filing of 510(k) or De Novo registrations for these EUAs? Or will the data need to be redone to CLSI standards?

Toby Lowe: And so I'm not sure I'm completely following that question. We have indicated on this call previously that we have authorized a De Novo and a 510(k). We've granted a De Novo and cleared a 510(k) for molecular COVID tests. And we do have feedback that we can provide either in a pre-EUA or if a developer emails the EUA mailbox, we have some feedback that we can provide on how to transition from an EUA to a 510(k) for molecular.

For serology and antigen tests, we do not yet have any tests that have received full marketing authorization. So we would expect the first one to be a De Novo. And hopefully, at some point in the near future we will also have some additional feedback that we can provide on expectations for making that transition from an EUA to a De Novo-- excuse me, or a 510(k) for serology and antigen tests. Excuse me.

Erika Bladholm: Thank you.

Joseph Tartal: Our next question is from Homer. Homer, I'm unmuting you. Please unmute yourself, and ask your question.

Homer Wu: Hi, this is Homer Wu from Hopkins MedTech Compliance. Thanks for taking my call. We actually know this for the comparator, this is for the OTC antigen test.

For the clinical study we noticed that FDA recommend we use the nasopharyngeal for the comparator sampling method. But we do notice that in some cases if the study have not shown very well. So if they don't do that properly, we get a very high CT value. So I was wondering, can we have to use the nasopharyngeal? Or can we use the anterior nasal swab for the comparator?

Toby Lowe: So I didn't quite catch what you said if something is not done right, then there's a high CT value. What was it that you were saying?

Homer Wu: Yeah, we noticed during our study if we-- our study stuff, if they don't do the nasopharyngeal very deep, if they don't do very well, even when we do the tests we get a very high-strung antigen results. But the CT value is still high, indicates the virus is low. So we're just wondering, can we actually use the nasal swab for the comparator?

Toby Lowe: So generally, I believe-- and Kris, feel free to jump in-- that we are using or requesting nasopharyngeal or mid-turbinate as the comparator. There are some cases where the CT values are higher with infections right now. And it may be useful for you to consider whether the staff that are performing the study and collecting the nasopharyngeal samples may need to perhaps have some better training for doing those collections.

Homer Wu: Yeah, so I mean because in the template it said we can't use nasal swabs. But it's recommended to use nasopharyngeal.

Toby Lowe: OK, so is your subject test using anterior nasal, the test that you're proposing?

Homer Wu: The test is using anterior, yeah.

Toby Lowe: Then, yeah, you can use anterior nasal as your comparator if you're subject test is anterior nasal.

Homer Wu: OK, OK. Thank you very much.

Toby Lowe: Sure.

Joseph Tartal: Thank you for your question. Our next question is going to be Don. Don, I'm unmuting your mic. Please unmute your mic, and ask your question.

Don Kafader: Yes, hi, thank you for taking the call. My name is Don Kafader. I'm with LabCorp. And with respect to the recent draft guidances that came out for the transition once the emergency is ended, the guidance documents dealt with IVD, manufactured IVD products and those under enforcement discretion. Can we be looking forward to any kind of guidance with respect to LDTs that currently are under EUA authorizations?

Toby Lowe: Thanks for that question. I know-- oh, sorry, sorry. I have an echo. All right, all right, let's if I can do this without-- can you all hear me?

Don Kafader: Yes.

Joseph Tartal: Yes, we can.

Toby Lowe: OK, sorry about that. I'm not sure what's happening there. So thanks for the question. I know it came up in yesterday's call as well. I would recommend doing [INAUDIBLE] for the [INAUDIBLE].

Don Kafader: I'm sorry. You're breaking up badly.

Toby Lowe: I'm sorry. Let me see what I can do about this.

Joseph Tartal: You're good now, Toby.

Toby Lowe: OK, is that better?

Joseph Tartal: Yes.

Toby Lowe: OK, thank you. So thanks for that question, and sorry for that sound mess there. So I would recommend that you submit that comment to the docket and note specifically that that's an area that could benefit from added clarity so that we can consider how best to provide that feedback in the final guidances.

Joseph Tartal: Don, does that answer your question? Please unmute yourself, and let me know if that answers your question.

Don Kafader: Can you hear me?

Joseph Tartal: Yes.

Don Kafader: No, that's fine. We'll submit the comment to the docket with respect to the draft guidances that have been issued. So thank you for your reply.

Joseph Tartal: Perfect, thank you.

Toby Lowe: Great, thanks.

Joseph Tartal: Our next question is from Sarah. Sarah, I'm going to unmute you. Please unmute yourself, and ask your question.

Sarah Beckman: Hi there. This is Sarah Beckman from GENETWORx. And I am just wondering for the LDT to EUA submissions that are currently under review, what's the appropriate mechanism or process to add amendments to those EUAs?

Toby Lowe: Sure. You can submit that the same way that you submitted your EUA request to begin with. So you can send that. If you already have a lead reviewer, you can send it to them and copy the EUA mailbox. If you don't have an EUA reviewer, a lead reviewer yet, you can send it to the EUA mailbox. Just make sure that you reference your EUA number that you should have received when you submitted your request to begin with.

Sarah Beckman: OK, great. Thank you.

Toby Lowe: Sure.

Joseph Tartal: Thank you, Sarah. Our next question will come from Sue. Sue, I'm unmuting your mic. Please unmute yourself, and ask your question.

Sue: OK, can you hear me?

Joseph Tartal: Yes, we can.

Sue: Thank you. My name is Sue Hartz from Phoenix Health, and I have two questions. Both are in regard to things covered in the beginning of this presentation. The first one has to do with the swab. Was this in regard to a swab that you yourself include in your test kit that you are intending to have in your EUA?

Toby Lowe: So that was responding to a question that we received ahead of time about generally just how to find swabs, I think. But in terms of a swab that you're including in a test kit, we would expect either that you use a previously cleared or legally marketed swab or that you provide information about the swab and how you are controlling for it in your test system.

Sue: OK, OK. And my next question—[INAUDIBLE]. What was that?

Kristian Roth: I think those are the two options. So you use a swab that's already available legally. Or if it's not, then you bring it under your quality system as a component of your test. And it would be—

Sue: If you're bringing one in that's not already on the market in the US is what I was asking.

Toby Lowe: Yeah, and so that's where we would expect you to bring it in under your test system as a component.

Sue: OK, and the next question has to do with the sample sequencing of your clinical samples for EUAs submitted after January 12. Is it possible to provide as an alternative statistical data from CDC that indicates the percentage of the strains in the population during the time frame of your clinical study?

Toby Lowe: So generally, no. For antigen tests, we have emphasized the need for direct sequencing of those positive samples due to some variability that we have seen with antigen tests.

Sue: OK, thank you very much.

Joseph Tartal: Thank you. Our next question is from Geetha. Geetha, I'm unmuting. Please unmute yourself and ask your question.

Geetha Rao: Thank you. I have a follow-up question from a couple of previous answers you provided on the timing of the EUAs. So the situation is that we had an LDT for which we provided a request for a notification. We're basically receiving the biweekly updates, and we're still in process.

We have not yet been assigned a lead reviewer. Then based on a previous feedback I got on one of these town halls, we submitted a follow-on EUA. We referenced to the original EUA. We followed requests to do some modifications and expansions. However, we received a new EUA number for that one. It was not attached to the original EUA. So we currently have two in process. And what we would like to do is two more things, and I'm really worried about the EUAs stacking up.

One is we'd like to add a sample collection kit for home collection. Currently, it's a point-of-care device. And I assume that we should be able to do that as an amendment to the second EUA, which is the

expanded EUA. And then the additional other activity that's planned and, again, something we have talked about in an earlier town hall is to relocate the CLIA lab to a larger facility because it's a very high-throughput lab. And we do still need a larger facility. And we have been told to check in with the FDA prior to the relocation. And we're getting closer to that time.

So my question is, do we still attach these to the first or the second EUA? Do we try to consolidate everything and then the timing that we can expect for all of this?

Toby Lowe: Yeah, thanks for that. That's some very specific to your case questions. So I'm going to give you a little bit of feedback, and then I'm going to ask that you send an email to the EUA mailbox. And you can ask. You can either copy me or ask that it be sent to me, and we can try and get some resolution.

If your intent was for your follow-on request to be part of your original EUA request, you can send a note saying that this was intended to be an amendment to the previous request and ask that they be consolidated into a single EUA request. And if you're submitting additional information to that EUA request, you can again make clear in your email that it's an amendment to EUA number whatever and ask that it be added to the same request, not logged in as a new EUA request.

You mentioned that this is currently point of care. If it's--

Geetha Rao: The collection is point of care, to clarify. The collection is point of care. We would like to provide a home collection kit.

Toby Lowe: Gotcha.

Geetha Rao: It's still a lab test. The test is still processed in the CLIA lab.

Toby Lowe: So the high-complexity CLIA lab, got it.

Geetha Rao: Yes.

Toby Lowe: So yeah, so you should be able to submit all of those requests as long as this is the same test. It's a single test. Then you can submit everything under the same EUA request. And it will all be considered as part of the same submission once you're assigned a reviewer.

Geetha Rao: Oh, great, great. Thank you. Yeah, and I'll send a follow-on email about that, and I'll ask about the relocation. We've just been-- we're just relocating the facility.

Toby Lowe: Yeah, that can go in the same EUA request as well.

Geetha Rao: OK, terrific. Oh, great. Thank you. Thank you very much.

Joseph Tartal: Thank you. Our next question is from McKenzie. McKenzie, I'm going to unmute your mic. Please unmute yourself and ask your question.

McKenzie Cato: Thank you. This is McKenzie Cato from Hyman, Phelps, & McNamara. I understand that 10% to 20% of the positive specimens in clinical validation of antigen tests must be low positive. But if

that percentage are not collected prospectively is it generally acceptable to supplement the study population with some additional contrived low-positive samples using spiked confirm negative specimens. Or is that not possible for antigen tests?

Toby Lowe: So I'm going to see if Kris wants to add anything to this. But generally at this point in the pandemic, we are asking that specimens be true clinical specimens not contrived for your clinical study. And as we mentioned earlier, there are various ways to enrich your study. And we can discuss that specific to your situation in a pre-EUA.

McKenzie Cato: OK, thank you.

Toby Lowe: Did you want to add to that, Kris?

Kristian Roth: Yeah. You know this does come up from time to time. And I think it really kind of depends on characteristics of your study. And we're glad to find a path forward. And I think there's a couple of different solutions.

Certainly, we don't want to get into this infinite loop of enrolling more folks and then chasing that 10 or 20 percent as you get more positive. I think we recognize that. So I can't give you any specific recommendation right now, but I think there are avenues that we could help.

McKenzie Cato: Thank you very much.

Joseph Tartal: Thank you, guys. And our next question is going to be from Annie. Annie, I'm unmuting your mic. Please unmute yourself, and ask your question.

Annie Wright: Can you hear me now?

Joseph Tartal: Yes. I can hear you.

Annie Wright: Hi, hello. This is Annie Wright from [INAUDIBLE] USA. My question is regard to a molecular diagnostic test for point of care.

We are in the midst of trying to file EUA, and we're trying to figure out which template to use for the submission. And there doesn't seem to be there's one specifically for molecular point of care. Do you have any recommendations on how we go about determining?

Toby Lowe: Yeah, so there is a molecular-- there's a general molecular diagnostic template. And that does have recommendations for both lab-based and point of care. So you can use that.

I believe the title is just molecular diagnostic template. You can use that along with the molecular diagnostic EUA cover sheet template. And then just look for the recommendations that are specific for point of care. And Kris was telling me that it's in section 12, page 30. Thanks, Kris.

Annie Wright: Was this released in 2020 or 2021? Because I looked at the 2021 version, and I didn't see.

Toby Lowe: October 6, 2021 is the one that's currently linked on our website.

Annie Wright: Oh, my killer. OK, let me-- I'll take a look at again today. OK, thank you so much.

Toby Lowe: Sure.

Joseph Tartal: Thank you our next question will be from Sam. Sam, I'm unmuting you. Please unmute yourself, and ask your question.

Sam: Yes, hello, thanks for taking my call. Can you hear me OK?

Joseph Tartal: Yes.

Sam: So this is Sam Ali from Intune.bio. I have a question. It's more of a comment, actually.

So we do trials, clinical trials, for sponsors. And some of them are from outside the US. And as we all know, all the self-testing trials must be run in the US. But from experience several times bringing supplies tests from outside the US has been such a pain, going through customs and clearance and going through FDA holds on the supplies, lots of questions about what the intended use and all these even though we provide all the information indicating that these tests are for investigational use with the codes and all.

But it's still-- as an example, currently we have a trial. And everything is ready, the protocol, IRB approvals, and the sites and everything ready. But it's been 10 days. We're waiting for the supplies to come in and cleared by the FDA.

So I would like to know there if you have any recommendations either to us as sponsors and CROs and also maybe internally to make some recommendations within the FDA to accelerate the process and realize that there's some urgency there to get the supplies quickly.

Toby Lowe: Yeah, so I believe that there is some information on our website about how to appropriately label the product for import for investigational use. If you're having difficulties with clearing the imports, you can send an email. And our group doesn't directly handle imports, so I'm not going to be able to give you super helpful advice. But we can definitely get your email over to the imports group if there's a hold up there.

Sam: OK, I appreciate it. Thank you very much.

Joseph Tartal: Thank you. Our next question is going to be from Bryan. Bryan, I'm unmuting you. Please unmute yourself, and ask your question.

Bryan Johnson: Hi, thanks for taking my question. Can you hear me OK?

Joseph Tartal: Yes.

Bryan Johnson: Thank you. This is Bryan Johnson from again from Beckman Coulter. Thinking specifically about serology assays, will there be any new clinical study requirements either in the templates or the guidances specifying the need for variant testing? And if so, will a panel of variants be recommended including vendor information? Or will the FDA issue additional criteria to establish a robust variant clinical study for the submission?

Toby Lowe: So we do have some information in the templates regarding variant testing. Generally, it is at a high level that we do expect developers to consider the variants that are currently circulating and to have a plan for ensuring that their test is not negatively impacted by future potential variants. So given that things are changing, having that plan is really the critical part and not necessarily forever specifying a specific panel. But Kris, I don't know if you want to add to that from your perspective there.

Kristian Roth: No, I think you covered it. Thank you.

Toby Lowe: OK, great.

Bryan Johnson: Yeah, and the second part of my question was around robust clinical study criteria, performance criteria. Can we expect anything more along those lines?

Toby Lowe: And so the templates do include our performance expectations for clinical studies. So if there's a specific question that you have about the templates that's unclear, we're happy to answer that.

Bryan Johnson: OK, I'll hold that question for a future town hall, I think.

Joseph Tartal: Thank you. Our next question will be from Rainer. Rainer, I'm opening up your mic. Please unmute yourself, and ask your question.

Rainer Ziermann: Hello, hi. This is Rainer Ziermann. Can you hear me?

Joseph Tartal: Yes, we can.

Rainer Ziermann: Great, I have a question about the use of a serology test. Specifically, if a serology test is authorized for nasopharyngeal swabs and the intended use clearly calls out nasopharyngeal swabs, can I assume it's OK to use it also for anterior nasal swab since FDA typically considered nasopharyngeal swabs as the most challenging sample type? Or are there any concerns?

Toby Lowe: I'm sorry, did you ask her about a serology test? I don't think that we have any serology tests for nasopharyngeal. I think they're typically for blood samples. I just want to make sure—

Rainer Ziermann: No, they are. I mean, I can tell you the name. But there is one particular test if you would like to use. And its intended use is specifically only authorized for nasopharyngeal swab, at least at the sample type that's listed. But we want to use it for anterior nasal swabs.

Toby Lowe: So I'm not familiar with a test that we've authorized for serology for nasopharyngeal. So if you can send that into the mailbox, we can take a look.

Rainer Ziermann: So in general, you wouldn't automatically say that it's OK if-- I mean, I can send it to you, of course. But I always assume when you have nasopharyngeal swap as the sample type, anterior nasal swabs can be used as well.

Toby Lowe: So for molecular tests, we have typically authorized multiple respiratory sample types if nasopharyngeal is studied. But the tests should always be used according to their authorization. So if it is

only authorized for nasopharyngeal, there may be a reason why. And, again, I don't believe that we have any serology tests authorized for nasopharyngeal. So that definitely would need to be looked at.

Rainer Ziermann: OK, thank you very much. I'll send an email. Thank you.

Joseph Tartal: Our next question is for Jennifer. Jennifer, please unmute yourself, and ask your question.

Jennifer Stanford: Hi, this is Jennifer from Hopkins MedTech compliance. Quick question, we're doing over the counter, rapid antigen studies. And it was our impression through the template that the FDA prefers the order of the self-test versus the NP swab be alternated to show randomization between patients getting these tests conducted.

Is that an accurate statement? And do you have any guidance on that? Because we do have multiple sites around the country with different collectors, so we just want to make sure we're meeting your guidelines.

Toby Lowe: Yes. I think this is a question that came up earlier on the call as well. If the comparator is not being used for standard of care, then randomizing between which one goes first is beneficial. And there should be some information in the templates, I think, that discusses this. So I would recommend that you take a look at that.

And if you have a specific question or want to specifically confirm in your situation that you're running your studies as we would recommend, you can send that it to the mailbox. And we can take a look. If it's quite in depth, we would recommend a pre-EUA.

Jennifer Stanford: OK, great. Basically, we are just-- because there are so many different people collecting samples that we're having each person collecting randomize their order. So one, then the other, one, then the other, and mark that down on their source document as to which one they did first to show due diligence across the board that we are trying to do randomization. That seem reasonable?

Toby Lowe: Kris, do you want to weigh in on that? Or should we have that go to the mailbox so that their review team can plan?

Kristian Roth: Yeah, thanks, Toby. I mean, on the surface, it does. Some folks have used year of birth to be more prescriptive about which one. If you're an odd year, you take the comparative first. If you're in an even year, you take the candidate device first.

Leaving it up to the individual, I'm not sure if that's going to get you truly randomized. And then, are you using or are you recommending some wash-out period? That's always a question as well. If they take a sample back-to-back, then [INAUDIBLE].

Jennifer Stanford: Well, and those are all good questions and gray areas that we're trying to operationalize as we go and try to be consistent. So I hadn't heard that year of birth as an option. But the way we have it written in our protocol is that each collector will alternate, and then they document that. So I feel like that's about as good as you can do when you have people collecting all around the country. You don't know who's doing which order necessarily.

But then you know the other point you brought up is interesting regarding the, how long do you wait? Because if you're doing an anterior swab for your over-the-counter test and then you're doing an NP swab to compare it to, does there need to be a wait period? I don't really know if there's a good answer to that.

Kristian Roth: There likely isn't. But we haven't really recommended that. We consider those two different anatomically separate areas. So I don't think there'd be at least depletion of material from the anterior. But that being said, it depends on how conservative you want to be in your sample, right? If you really want to make sure that they're not interfering with each other, it may be helpful.

So I think if you have a sampling plan that you want to discuss with us, you can send that into the inbox. And we can send that to the antigen team directly. And they would be able to answer this very quickly for you.

Jennifer Stanford: OK, great. Thank you.

Joseph Tartal: Thank you, Jennifer. We have time for one last question. Zakir, I'm opening up your mic. Please unmute yourself, and ask your question. This'll be the last question.

Zakir Murtaza: Hello.

Joseph Tartal: Hello, we can hear you.

Zakir Murtaza: Hello, yeah, this is Zakir from Applied Biomedical. I would like to know about this variant. We have done a sequence only for omicron, not for other variants like delta and others. So that only sequence for omicron is more than enough, or we have to do other sequences also in our sample testing?

Toby Lowe: So for the current recommendations for antigen tests, we are recommending sequencing for all positive specimens. And in terms of --

Zakir Murtaza: In other words that we should have in our sample all variants, basically, right?

Toby Lowe: No, we're suggesting that you perform your clinical study and any results that come back positive, you sequence them.

Zakir Murtaza: For all of them?

Toby Lowe: All positive--

Zakir Murtaza: Basically that's what the recommendation. Is that right?

Toby Lowe: Yes, all positive specimens for an antigen study to be sequenced.

Zakir Murtaza: All of them, OK. So yeah, I mean, we sequence only for the omicron. So we sent 10 samples from that, and we got 7 out of 10. So we thought that we completed the omicron. So according to you we should have all the other as well for sequencing.

Toby Lowe: So before you sequence them, you wouldn't know what the variant is.

Zakir Murtaza: Right, that's true.

Toby Lowe: I'm not quite sure that I'm understanding the question. We're not asking that you have all variants in your clinical study. We're asking that you sequence all positives.

Zakir Murtaza: Oh, I see, OK. OK, I see. So we were thinking that we need to have at least a few omicron only. So we start with-- the first time, we got a few omicron so we thought we covered everything. So according to-- so we have to have all the sequence for all the rest of the samples. OK, very good. Thank you.

Joseph Tartal: And with that, that is our last question of the day. So thank you, everyone. We greatly appreciate your participation. Thank you, Toby, and thank you, Kris, for all the answers to the questions.

Today's programs and transcripts will be made available at CDRH Learn. Please visit CDRH Learn at www.fda.gov/training/cdrhlearn. You will find the recording and transcript in the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. For additional questions about today's program and COVID IVD topics in general, please email CDRH-EUA-Templates@fda.hhs.gov.

As we continue to hold these virtual town halls, we appreciate your feedback about the program series. Please complete a brief survey, which you will find at www.fda.gov/cdrhwebinar. Also, please remember to join us for the next IVD town hall scheduled for Wednesday, March 9, 2022. And this concludes today's program. Thank you.

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