Virtual Town Hall #73
November 17, 2021

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 73 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in the fight against 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. Please note, all previous recordings and transcripts are available.

The next IVD town Hall will take place next month on Wednesday, December 1. Our panelists for today's program are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health, or OIR, 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.

We will start with opening remarks from our speakers and a presentation on the recent updates for COVID-19 testing, including the revised guidance document "Policy for Coronavirus Disease 2019 Tests During the Public Health Emergency" that posted Monday, November 15th. Then we'll open the program to your live questions.

Since we have this presentation today, we will not cover any of the questions we received by email for today's town hall. We are working on getting written responses sent back to each of those inquirers. So please be patient, as we should be able to get an email response to you by the end of the week. Now I'll hand the program over to Toby. Welcome, Toby.

Toby Lowe: Thanks, Joe. Thanks, everyone, for joining us again. We've had several updates-- or we have several updates to share with you since the last town hall about a month ago. This was one of the longer breaks we've had in between town halls.

And as Joe mentioned, we will go through some intro updates, and then we will get into what folks are probably very interested in with Monday's actions that's just showing now up on the screen. So in addition to the actions that went down on Monday that we'll talk about in detail, I did want to point out that since the last town hall, we've had some template updates.

We updated the molecular and antigen home use test template twice - once on October 25 and once on November 9. The first was to update the test labeling recommendations regarding additional indications for over-the-counter use, as well as flexible study recommendations for demonstrating usability.

And then the November 9th update was to update the performance recommendation for over-the-counter single-use tests for all patient populations to 80%. So that aligns with the performance recommendations for antigen tests for all patient populations in these settings. And then also with the October 25th update, did some corresponding updates in the supplemental template for serial testing.

We also, earlier this month, cleared the first COVID-19 test 510(k). And we have also issued several new EUAs for over-the-counter COVID-19 tests and reissued several to add additional indications. And those are all posted on our website, of course.

We also had a couple of updates. One for the Ellume test and one for the Abbott Alinity. Those were both class I recalls regarding the potential for false positives. And the details for those are also on our website.

And then, very importantly, I want to welcome Tim back to our town hall. He is back from some much needed time off, and we're glad to have him back here. So Tim, I'll turn it over to you to kick off the discussion on Monday's updates.

Timothy Stenzel: Thank you, Toby. It's good to be back. And I just want to give a heads up that I've got some construction going on in the background. There's some hammering going right now. So hopefully, it won't interfere with our conversation.

In today's town hall, focusing primarily on the HHS statement on Monday and the updated FDA guidance, this is the beginning of the conversation of these changes. I would just say that for any of the new provisions that apply to you, please note the dates that started. The clock started on Monday. And just be sure that you meet those dates.

But again, this is the beginning of the conversation. We don't expect that all questions will be asked and all answers will be given with these updates. And we want to make sure that we maintain a really close dialogue with developers who want to use these new pathways, particularly for LDTs, that were outlined in the guidance.

So with that, we'll start in with the slides. I'll do a couple of slides and then hand it back over to Toby. And really grateful that Kris is on as well. He did a great job-- both Toby and Kris – in covering when I was on my annual leave. And Kris rejoins us again today due to his outstanding technical expertise and background in this area.

So first of all, the Secretary issued a statement on Monday that most everybody is probably familiar with by now. But as of Monday, effective today, the HHS no longer has a policy on LTDs that is separate from FDA's long-standing approach in this area. We're going to focus on COVID right now. This is a COVID-related meeting.

There may be questions about other LDTs, and we might have to put those off for now. There's going to be a lot of questions. We're in a pandemic still, and there's still a great need for quality tests. So then we made some updates to the policy in the links for both statement. And the policy update are here, as well as press releases.

And I just want to quote from the press release or the public statement from the FDA. "By focusing on our review on-- tests that will have the biggest impact on the nation's ongoing COVID-19 testing needs, such as at-home and point-of-care diagnostic tests that can be produced in high volumes-- and helping you ensure the available tests have appropriate oversight, we can better respond to the pandemic as the nation's testing needs continue to evolve."

The next slide, please. So here's the reissued guidance link. And then there's four main policy areas covered in this updated guidance. One is prioritization of review of EUA requests for tests. That's Section IV.A. State authorization-- Section IV.B. Distribution and offering of tests during FDA review-- Section IV.C. And modifications to EUA-authorized diagnostic COVID tests-- Section IV.D. Next slide, please.

I'm going to reiterate that test accessibility remains our main focus. Those entities that have LDTs and are covered under the policies and the provisions in the updated guidance can remain on the market as long as they meet the requirements and submit on time if that is part of it. Then while the FDA is reviewing those , they can remain on market.

And then Toby will also go into detail about a new LDT umbrella policy that if it's followed, and the FDA is notified, essentially that LDT is immediately authorized. And Toby will go into more detail on that. So our priorities are listed here. And I just want to go through them. They're very similar to what they have been for a long time, but there are going to be some changes. And we can go through some of that.

So obviously, at-home and point-of-care diagnostic tests as antigen molecular for the use with or without a prescription and that can be manufactured in high volumes remain a high priority for us. And as our high-volume, lab-based molecular diagnostic tests and home collection kits for such tests that expand testing capability and accessibility. And pooling can be part of that. A home specimen collection, testing of specimens collected at home will be part of that, as well as screening individuals or detecting multiple respiratory viruses.

We're seeing a little bit of flu. The latest CDC report I saw said there were about 300 confirmed positives in the US through the CDC program. So unfortunately, it doesn't look like a lot, but we obviously are monitoring that situation closely. But we want to be prepared, and we want to support those multi-analyte tests. Also certain that lab-based and point-of-care high-volume antibody tests that can measure the amount of antibodies that is fully quantitative antibody tests or the amount of neutralizing antibodies.

And then finally, any test request that is from or supported by a US government stakeholders such as BARDA, or NIH, the RADx program, will remain a priority as it has been since day one. Next slide, please. And I believe that's when I turn it over to Toby.

Toby Lowe: Thanks, Tim. So thanks for that great intro into our recent actions. As Tim mentioned, I'll walk through a little bit of a deeper dive into the specific documents and what the details are there. But as always, the full details of the policy are in the posted documents online. So you should make sure to refer to those to make sure that you're getting all the nuances and details that we understandably cannot include in the slides and the presentation today.

So just some quick reminders that are-- there's some sort of clarifications that are outlined in the background and scope of the updated guidance. This first one we've had some questions about. The enforcement policies in the guidance do not address MDR. That's medical device reporting as covered by 21 CFR Part 803. So developers are expected to comply with applicable MDR requirements for tests that are offered prior to authorization as described in the guidance.

And then I know we've talked about the second one quite a bit. Unless and until an EUA is issued that authorizes additional testing environments, the test is limited to high-complexity CLIA-certified labs. And the policies regarding offering COVID-19 tests prior to or without an EUA have never applied to at-home

tests or tests with home specimen collection or anything outside of the high-complexity, CLIA-certified laboratory. And further, the notification policies have never applied to multi-analyte respiratory panels.

Next. So this is one of the flowcharts that's included in the guidance. This is in Appendix A, talks about the policies that are in Section IV.A of the guidance. And that's the section that talks about the EUA review priorities that Tim just went through.

So there's a lot of details here, but the gist of this is basically that you can go through and figure out what applies to your test and see where that would put you in terms of review priorities. For example, you can see for all three molecular antigen and serology and if it's a test that's supported by a US government program, as Tim mentioned, such as BARDA or NIH RADx, that would go directly to FDA intent to review.

Similarly, for antigen tests, if it's not supported by a US government program, and it's not a point-of-care or at-home, it's going to go straight intends to decline. And there is some discussion in the guidance about if you don't fit into one of the bullets about priorities, but you think that there's a reason why your tests should be prioritized, if it's a novel test for some reason, we would encourage you to reach out and discuss that with us.

All right, so moving on. The Section IV.B of the guidance talks about the State Authorization policy. This was discussed in the previous versions of the guidance. And we have updated it such that we no longer intend to apply the policy to any additional states or territories going forward. But those that are already listed on the notification list prior to Monday may continue to do what they've been doing all along.

So then Section IV.C of the guidance talks about distribution and offering of tests during FDA review. This is probably the largest section of the guidance, and the one that folks who have been operating under the notification policies previously are likely to be very interested in. So as everyone knows, the previous policies included the previous versions of our FDA guidance that had the notification policies, as well as the HHS August 2020 announcement, which, among other things, talked about LDTs for SARS-CoV-2 being offered without FDA authorization.

So under the updated policy, we generally expect COVID-19 tests to have been issued an EUA for a marketing authorization prior to the tests being distributed or offered. This goes along with HHS withdrawing their August 2020 policy. And as the guidance outlines, we are ending the notification policies going forward.

We do generally intend to review EUA requests for tests that were offered without an EUA request previously. And we have outlined timelines for which we intend for developers to submit those EUA requests. And then if a test is not subsequently authorized, we expect developers to cease marketing the test within 15 calendar days of being notified that we will not be authorizing their test.

Next slide. So here's the second of the flowcharts that is in the guidance. This is in Appendix B. And it discusses the policies in Section IV.C of the guidance that I just mentioned. So we can walk through this one a little bit because this does cover the timelines.

So this appendix is specifically for tests that were offered under the notification policies or under the HHS August 2020 statement without having submitted an EUA request to FDA. So it starts out-- you would look at whether or not an EUA request was submitted prior to Monday-- the updated guidance.

If you have not, then you would be expected to submit an EUA request to FDA within 60 days from Monday, from the 15th. If you do not submit an EUA request, then we would expect you to stop offering that test by the end of that 60-day time period. And if you do submit an EUA request, then we do not intend to object to you continuing to offer that test while we review your EUA request.

Then obviously, if your EUA is authorized, you can continue on with an authorized test. And if your EUA is not authorized, we would expect you to stop offering this test. Then if we jump back to the beginning and follow the other path, if you did submit an EUA request prior to November 15, then we would look at whether you submitted an EUA request before or after February 1.

So if you submitted your EUA request after February 1 you don't need to do anything. We will continue to review your EUA request. And you'll follow along-- you can continue offering it. If you get authorized, great. If you don't, you have to stop marketing.

If you submitted your EUA request before February we expect to hear from you within 45 days from Monday's reissuance to confirm that you still are offering that test or still want your test to be reviewed and to add any updated data, if needed. There are some EUA requests that have been in our queue for quite some time.

Often, these are ones that are lower priority based on our review priorities, but we want to make sure that the developer is still interested in authorization, and that we have all the current data. And then as long as we hear from you within those 45 days, we'll continue to review. If we don't hear from you within those 45 days, we would expect you to stop offering the test.

Next slide. So then, the next policy that's discussed in the guidance is regarding modifications. So there are discussions regarding modifications to EUA-authorized tests being offered prior to or without an EUA. Needs similar to the other policies have never applied to at-home tests or tests with home specimen collection or any testing outside of a high-complexity, CLIA-certified laboratory. The guidance includes recommendations for transparency regarding these tests; recommending that test developers include information in their test reports to make clear the modified test performance characteristics and to reflect the modification, and that the test has been modified and not yet reviewed by FDA.

And then similar to all other tests, if FDA identifies a significant problem or concern with a modified test, we would reach out to the developer to discuss it. And if it can't be addressed, we would expect the developer to cease distribution, marketing, and offering up the test and to address that problem. So that may involve a recall or other notification regarding selected test reports.

The next slide. So this section of the guidance breaks down the policy into those that are applicable to modifications made before November 15 and those made after November 15. So modifications made before November 15 that were made and implemented as discussed in the policies in the previous version of the guidance, we don't intend to object to a commercial manufacturer continuing to implement their modification while FDA reviews their EUA request, if the commercial manufacturer modified their own EUA-authorized test.

And then for modifications made and implemented by high-complexity CLIA-certified laboratories, we don't intend to object to continued offering of the modified test as discussed in the policies of the previous version of the guidance. And then for modifications made after November 15, we included

some additional details because this is an area where we had a lot of questions. And we wanted to provide some additional clarity in the updated version of the guidance.

So for those newer modifications, we are clarifying that this applies to changes that do not-- sorry-- to modifications that do not change the indication for use set forth in the EUA, and that do not change the analyte-specific reagents. And in those cases, we don't intend to object to modifications by a commercial manufacturer to its own EUA-authorized test being implemented while FDA reviews the EUA request, and for modifications made and implemented by a high-complexity, CLIA-certified laboratory, we don't intend to object to implementation of the modification without notification to FDA or a new or amended EUA, as long as the lab has validated the modification confirming equivalent performance, and the use of the test is limited to the high-complexity, CLIA-certified lab in which the modification was made.

Next slide. So that's pretty much the rundown of the guidance update. So now we can talk about the umbrella EUA that Tim mentioned. We did, concurrently with the guidance on Monday, issue a new umbrella EUA. It is for serial testing with certain molecular diagnostic tests developed by laboratories.

This is really geared towards use for testing regular intervals as part of a serial testing program. We know that there are a lot of those being established in schools, workplaces, communities, et cetera. And it provides an efficient way to authorize certain tests that meet specified criteria.

The umbrella EUA is for use with individual or pooled anterior nasal specimens; for testing individuals, including those without symptoms or other epidemiological reasons to suspect COVID-19 when tested at least once per week. And the umbrella includes different options in the intended use, including different numbers of pooled samples, media pooling, and swab pooling, and options to include testing with home-collected specimens.

The appendices in the umbrella EUA include the validation that's required in order for a test to be authorized for each optional indication. And all tests authorized by this EUA are limited to use in a single laboratory that developed the authorized test, and that is certified under CLIA and the requirements to perform high complexity tests.

Next slide. All right, so those are the primary things that took place on Monday. This slide lists out the additional actions that we had quite a few web updates, including most of the frequently asked questions. And we did reissue the March 2020 EUA for certain molecular diagnostic tests developed and performed by high complexity labs.

The reissuance essentially closes out this EUA. This was an umbrella. And now at this point, only the tests that are listed in Appendix A are authorized for use as described in the EUA. And no additional tests will be authorized by this EUA. And then the reissuance also updated the conditions of authorization in the fact sheets to reflect the most up-to-date information. And then there were a couple of conforming edits made to the VTM guidance to match the updates made to the test policy. All right.

Joseph Tartal: OK, thank you, Toby. And thank you, Tim. Now let's open the program up for some live questions. We will only be taking live questions by phone or by connection. 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. I will unmute you. Then you need to unmute yourself and ask your questions, identify yourself. Please, only one question at a time. Also please no questions about specific submissions.

With that, we are going to take our first question of the program. Shrikar, I'm are unmuting you now. Please unmute yourself and ask your question.

Shrikar Tatapudi: Hi. Thanks for the opportunity. This is Shrikar from UserWise Consulting. We specialize in human factors for medical devices. So we're currently conducting usability testing on a molecular COVID-19 IVD as an over-the-counter OTC use product. We're also separately conducting an OTC clinical evaluation study.

But with regards to the usability study, the new template calls for 15 participants testing themselves and 15 participants testing another person, child, or adult, depending on your intended use population verbatim. So we interpret the template to indicate that as long as we have some young adults aged 14 to 24 in the cohort of 15 participants testing themselves, we do not need to test young adults as a separate user group of 15 young adults. Does the Agency agree?

Timothy Stenzel: Toby, are you the best one to answer this or is it Kris?

Toby Lowe: I'm going to see if Kris is able to answer this. But if not, we may need to ask that that question be sent by email so that we can make sure that we check the language and the template and get the right answer.

Kristian Roth: Yeah, I think that would be best. Thanks, Toby. It sounds reasonable. But you want to make sure that we're getting, of course, the details right and cross-check that with the template. So if you can just send that in the inbox, or you can also just sent to me directly. And we can get you an answer on that. OK, thanks.

Timothy Stenzel: Yeah. Send it to the email box and ask them to forward it to Kris, and he'll make sure that you get a rapid response.

Shrikar Tatapudi: Thanks for answering that. We had already sent an email, and we will just forward it again. Thanks for answering that. Thanks.

Timothy Stenzel: Yeah, with attention to Chris will get it to the right decision maker as quickly as possible and get you a faster answer. Thank you.

Shrikar Tatapudi: Perfect. Thanks, guys.

Timothy Stenzel: Yep.

Joseph Tartal: Thank you. Our next question is from Riley. Riley, I'm muting your phone. Please unmute and ask your question.

Riley Doherty: Hello. My name is Riley Doherty. Thank you so much for taking my question. I am working with a company that's running a clinical study. I was wondering do you have any recommendations for how to find COVID-19-positive participants?

Timothy Stenzel: This is Tim, I can start off. Well, unfortunately, there's still a relatively high number of individuals in the US who are testing positive, and it may be rising. We hope that that's only a temporary blip. Can you tell us a little bit more? Again, I may have missed it, but what is the indication? Do you have a point-of-care test? Do you have an OTC test, or a central lab test? What kind of test do you have?

Riley Doherty: It's an over-the-counter home-use molecular diagnostic kit. And we've been running the test at our facility in our office, but we've struggled to find COVID-19-positive participants. However, we know this is a requirement in the FDA template to have at least 30 positive participants in a clinical study for OTC. So since we're having some trouble finding positive participants--

Timothy Stenzel: Where are you--

Riley Doherty: Go ahead.

Timothy Stenzel: Where are you based? What state? Are you near a major city? Where are you located?

Riley Doherty: I'm in the San Francisco Bay Area.

Timothy Stenzel: OK. So certainly a large area. The folks that have been most successful in getting samples usually have one site and/or do it fully at home by sending it to the home of this-- so Kris or Toby may have some additional suggestions.

But unfortunately, there's enough positivity out there. It's you connecting with patients who have symptoms so that you can get the testing done.

Riley Doherty: That makes sense. I think, from the way we see it, the population of positive is less than 5% in the US. So we've just had a harder time. We would have to sample a very large sample size. So any additional recommendation you have would be super helpful.

Timothy Stenzel: Well, we have used enrichment techniques, but I think we still recommend that if you use any sort of enrichment technique, that you run that by our team so that we make sure that it's not biased. But Toby, go ahead.

Toby Lowe: Yeah, I was going to say there is discussion about enrichment in the templates, so you can take a look at that. And then if you have specific questions about a proposed enrichment strategy, you can send those in either to your lead review, or if you have one such as for a pre-EUA or through the mailbox.

Riley Doherty: OK. Thank you so much.

Joseph Tartal: Thank you. Riley. Our next question, Madhav. I'm unmuting you. Please ask your question. Unmute yourself and ask your question.

Madhav Makkena: Hi, can you hear me?

Joseph Tartal: Yes, we can.

Madhav Makkena: Hello. Hi, I'm calling from MedMira. And is the FDA planning to update the templates for serology and antigen testings that were last updated in October on the 6th to reflect the changes that were made in the policy update yesterday, or day before yesterday?

Toby Lowe: And so the October updates--

Timothy Stenzel: Go ahead, Toby. I was going to suggest you speak to him. No, I going to suggest you speak to him.

Toby Lowe: Yes, so those updates-- if you see something in there that you think is not consistent, please reach out and let us know. But generally they should be fairly consistent with the updates in the guidance.

Madhav Makkena: In particular, what I was concerned with was the new policy update mentions that for diagnostic tests-- particularly, sorry, for antibody tests, you're focusing on quantitative detection of antibodies or neutralizing antibodies. Our test is a vertical flow-through antibody test.

So I was wondering how FDA's current thinking in terms of quantitative tests would apply to a qualitative test? And if you had any guidance for manufacturers making vertical flow antibody tests?

Timothy Stenzel: Our focus is primarily on fully quantitative tests and neutralizing antibody tests. So if your technology can be amenable to that, it may be important for our staff to hear some details about your technology to more specifically guide you.

Toby Lowe: Yes, agreed. And the templates do address recommendations for those fully quantitative tests and for neutralizing antibody tests. So you can see those recommendations in the October 6 versions of the template.

Madhav Makkena: Thank you.

Timothy Stenzel: And I would also add that we constantly look at and discuss with others in the U.S. government about what are the key testing priorities. And we have the ability to update the priorities. But these are the priorities that we see at this point in the pandemic; and then focus our FDA oversight and review to those that make the most difference at this point in the pandemic.

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

Rui L: Hello, this is Rui. I'm from an IVD manufacturer called Wonderful USA. So my question is that we are trying to finalize our OTC rapid antigen test format. And we have a question regarding the sample collection swab. Does FDA or EUA require the sample collection swab to hold a separate or independent 510(k).

Timothy Stenzel: Toby, you're really good at answering this kind of questions. Go ahead.

Toby Lowe: Sure. So we do expect that all sample collection devices should be legally marketed. So this means generally that they're either cleared or authorized. Or depending on the type of device, they may

be 510(k)-exempt. And then they would not need pre-market review, but would need to comply with other relevant regulatory requirements.

If you're proposing to use a collection device that is not legally marketed, we would expect to see sufficient information regarding the collection device in the EUA request. And then as the EUA sponsor, you would take regulatory responsibility for the collection device through your EUA.

Timothy Stenzel: And it is a legally marketed swab. We would obviously like to see how it performs with your specific test in the studies.

Rui L: So because this is also related to supply chain, so that means if the swab that we decide to use is not independently 510(k)-cleared-- but you also mentioned it could be a 510(k)-exempt. So does that work? Or should we provide the specific information if it's not 510(k)-cleared?

Timothy Stenzel: You can send in specific information to our template email box. Many are exempt. And all that is needed then is for you to demonstrate that the swab works with your test in the clinical studies and any other studies where that's important.

So I think if you have a specific swab in mind, I think the best thing to do is to send in a question to our templates email address, and we'll try to focus on that. And we do understand the important need to address supply chain issues. So we certainly want to be as flexible as possible.

Rui L: OK, great. Thank you. Thank you, team. Thank you, Toby.

Joseph Tartal: OK, our next question is from Sam. I'm unmuting you. Please ask your question. And we'll go from there.

Sam Ali: Yes, hello. Can you hear me?

Joseph Tartal: Yes.

Sam Ali: OK, thank you. So I have a question. It's about a multiplex, multi-analyte molecular test for SARS-CoV-2, as well as flu A and B. And the question is should the test, or must that test, differentiate between flu A and B? Or can the flu A and B be detected as a single target?

Timothy Stenzel: Kris, do you want to-- Toby and I have answered this before. But Kris, you're on the phone--

Kristian Roth: I apologize—

Timothy Stenzel: --so maybe you want to answer that?

Kristian Roth: Yeah. Thanks, Tim. Currently, I think the recommendations were getting both internally and externally are asking for differentiation of flu A and B and any flu test. So that's kind of the current opinion we're operating under. And we certainly encourage you to design your test that way.

If there's other arguments you want to bring to the table, I think we're open to listening to them. But I think we do have pretty solid opinion on differentiation from these types of tests.

Sam Ali: OK, all right, what's the value for differentiation, for reporting incidence and prevalence?

Kristian Roth: It's been discussed quite a bit in panel meetings. And we have input from CDC as well. Of course, reporting it is a clear benefit. But again, I don't think I'm going to get into the benefits and risks of differentiating here. Just to let you know that is a recommendation. And it is—

Sam Ali: I understand.

Kristian Roth: All right, thank you.

Sam Ali: Thank you.

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

Tom Alexander: OK. Thank you. Tom Alexander from Filmetric Diagnostics. My question refers to report language that we should use. We currently have a serology LDT that, on our report format, we state that it is an LDT and has not been subject to an EUA.

But now do we change that to say an EUA is pending after we make our application or we've submitted an EUA application? Or we're working on the EUA application for the time being with the new guidance? Any suggestions you have regarding our report format would be appreciated.

Timothy Stenzel: Toby, do you have prepared thoughts about this?

Toby Lowe: Yeah. So the guidance document does discuss in the Section IV.C, I believe it is, what our recommendations are for labeling and for making this clear. So generally, without seeing the exact language that you've been using, it's hard to say for sure, but it sounds like you may not need to change it. We would generally recommend that you just make it clear that the test has not been reviewed. And we do not recommend that you include any language that states or implies that EUA issuance or FDA authorization is imminent or pending.

Tom Alexander: OK, thank you very much.

Joseph Tartal: OK, thank you, Tom. Our next question is from Brittanie. I'm unmuting your line. Please unmute yourself and ask your question.

Brittanie Clarke: Hi, thanks for taking my question. This is Brittanie Clarke calling from Plexus Labs. Our lab is aware of MTMs, which have yet to clear 510(k) review. And we are looking to understand what the agency expectations at this time are during the public health emergency.

So can an MTM for investigational use only be validated by a lab? And if so, to what extent can this transport media be used after validation by the lab?

Timothy Stenzel: When you say for investigational use, can you give us a few more details? Is this product development that would be submitted to the FDA all under clinical study or trial? Can you give us a little more detail so we can make sure we're addressing your question properly?

Brittanie Clarke: So I'm not entirely certain. It's not yet submitted for 510(k) review for clinical use, if that helps clarify.

Timothy Stenzel: So you're planning that. You're doing a study. And you would use something that isn't legally marketed as transport media?

Brittanie Clarke: No study. Our lab is thinking about developing such media in-house. And we're just looking for some clarification, and what the enforcement discussion is.

Timothy Stenzel: OK. Toby, do you want to handle this one?

Toby Lowe: Yeah. So I think your best bet is going to be to send some details into the mailbox. But generally, we did issue a guidance document on viral transport media and providing some enforcement policies there for transport media that have not been cleared.

However, without knowing the details of yours specifically, generally, MTM is used to refer to transport medias that contain guanidine and/or other inactivating substances. And those do not fall under the policies in the VTM guidance. So it's unlikely that is something that we would think should be used without clearance. But you're welcome to send in more details to the mailbox so that we can consider your specific question.

Brittanie Clarke: OK. Thank you.

Timothy Stenzel: And I will say that that's something that, following authorization, can be used. We want to understand that. I mean, if you're doing a clinical study, and it's blessed by the IRB, we don't interfere with that. It's only when it comes to our review or is it something that's appropriate. And I think you want to de-risk what you're doing and make sure that what the path forward is to bring something to market like that. And that's what we're suggesting is to come in with an email through the template email address, and engage with us on that.

Brittanie Clarke: Got it. OK, thanks so much.

Joseph Tartal: OK, thank you. Our next question is from Venkateswaran. I'm unmuting your mic or your phone right now. Please unmute yourself and ask your question.

Venkateswaran Kodumudi: Good afternoon. Thanks for taking my call. Thanks for providing the information and additional discussion about the guidance. My question is related to the Appendix A. It is mentioned about high manufacturing capacity, then lab based, the high throughput capacity, and then for the instrument in a sufficient instrument and peak production capacity. So can you give additional information about what constitutes high manufacturing capacity and high throughput capacity, please?

Toby Lowe: Yeah. So seeing that we do have several other questions, I don't want to get into all the specific details here, but that just goes back to where I had mentioned that the flowcharts don't include all of the details, and of the slides do not include all the details. So I would have you go back and look at Section IVA of the policy, which does include the specific information that you're asking about. Primarily in footnotes, it includes details about what we mean by each of those phrases.

Venkateswaran Kodumudi: Thank you.

Toby Lowe: So I think-- yep.

Joseph Tartal: OK, thank you. We're going to take maybe another one or two more questions. Our next question up. Khasim, I'm going to unmute you. Please ask your question. Unmute yourself and ask your question.

Khasim Ali Khan: Thank you. Yes. Hi, I'm Khasim Ali Khan from BTNX. Question would be we're working on two types of antigen tests for OTC use, and we're in the process of beginning a clinical trial. My question is kind of follow up from the earlier discussion about the inclusion criteria.

When Tim pointed out that we could go to areas with symptomatic population, how does that suffice to the all comers aspect when we're including symptomatic population? Maybe I'll just pose a question and then you can let me know. Would this go through the route of first-symptomatic claim for OTC with a post authorization condition for asymptomatic screening without the data for asymptomatic, and then we work towards completing the asymptomatic population?

Timothy Stenzel: So there are two clear pathways for OTC. One is to only test symptomatic individuals. And if your performance meets the criteria for the serial testing plan, you don't have to do any more pre-market clinical studies. And there is just a post-market commitment to validate your serial testing in the asymptomatic population.

If you want to go for a single test claim for asymptomatic screening, then, yes, we do need to see data on asymptomatics. But the fastest way to market is to do symptomatics only, meet the performance criteria, get the authorization, and then agree to the serial testing plan.

I mean, antigen tests, typically, if you're going to get the maximum benefit from that-- and there are now a number of these-- it is important to do that serial screening because, if not, you are going to be less sensitive than a molecular test. And this applies to early in the infection.

We have data that says that you become molecular positive before you become antigen positive, and in many cases when the antigen test at that time is negative. And obviously, if the antigen test is positive, that's fine. But when the antigen test is negative early on in the infection, it's going to lead somebody to think that they're negative when they're just about to spike in their viral loads and viral production, and will most certainly be infectious, so. OK?

Khasim Ali Khan: OK. So yeah, I think the clear pathway to move forward would be to complete a clinical study for symptomatic population. And once that hits the performance criteria, we can request the serial testing for asymptomatic or the post-authorization claims can follow, right?

Timothy Stenzel: That sounds good to me. But it's up to you which pathway you go, but that would be the one that I recommend because it gets you to the market the easiest with the smallest amount of clinical data.

Khasim Ali Khan: Absolutely. Perfect. Thank you, Tim.

Joseph Tartal: Thank you. Next will be the last question of the program. I'm going to unmute you, Laura. Laura, please ask your question.

Laura Ferguson: Hi, Laura Ferguson from Delphine Diagnostics. We have a Section IV.C notification acceptance. And we have an EUA that was submitted prior to the February 1st date stated in the new guidance for review of our EUA and under notification policy.

But since the original EUA was posted and was actually under active review, and we received the notification acceptance, we resubmitted the EUA with all of our updated data. Should we use that resubmission date with the updated data as our date, and consider that we're not on the 45-day window? Or should we consider we're on the 45-day window given that the original EUA was submitted prior to February 1?

Toby Lowe: I would say just to make sure that we know that you want your EUA to be reviewed, go ahead and send us an email affirming that. I don't know offhand which date will be most prominent in our system. And I don't know if you've had those submissions as separate EUAs or within the same way. If they are separate, please include both EUA numbers in your email when you submit it.

Laura Ferguson: OK, will do. Thank you.

Toby Lowe: Sure.

Joseph Tartal: OK, with that, that wraps up our program for today since we're at time. So thank you, everyone. We greatly appreciate your participation. Today's presentation and transcript will be made available at CDRHLearn. Please visit CDRHLearn at www.fda.gov/training/cdhrlearn.

You will find the recording and transcript in the subsection titled "Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series." Again, as previously noted, all the recordings and transcript, except for today's, are now available and we will work on making today's recording and transcript available as soon as possible.

As I talked about throughout today's program, for additional questions about today's presentation and topics, please send an email to 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 may find at www.fda.gov/cdrhwebinar. Last, as a reminder, please join us for the next webinar, which is scheduled for Wednesday, December 1. This concludes today's town hall. Thank you very much.

END

****