

Virtual Town Hall #86
June 1, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kimberly Piermatteo: Hello and welcome everyone to Virtual IVD Town Hall number 86 for SARS-CoV-2 test developers and which we'll discuss and answer your questions about diagnostic tests in response to COVID-19. Thank you for joining us today. This is Commander Kim Piermatteo of the United States Public Health Service. And I am the Education Program Administrator within the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. I'll be your moderator for 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.

Our May 18th IVD Town Hall recording and transcript have been posted and the next scheduled IVD Town Hall will be on Wednesday, June 15th 2022 from 12:05 to 1:00 PM Eastern Time.

Our panelists for today's Town Hall are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics which is also referred to as the Office of Health Technology number seven or OHT7 in CDRH's Office of Product Evaluation and Quality. Joining Tim today is Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices also in OHT7.

For today's Town Hall we will begin with some opening remarks, followed by answering your previously emailed questions and then proceed to address your live questions. I'd now like to welcome Tim who will provide our opening remarks.

Timothy Stenzel: Thank you, Kim. And welcome everyone to this June 1st session. So some good news for those test developers out there who are seeking non-COVID IVD Pre-Submissions. So as of today, CDRH and our office plans to accept all non-COVID IVD Pre-Submissions in addition, previously, we were accepting COVID IVD Pre-Submissions. Specifically, at the beginning of this year we began again reviewing PMA Q-Subs as well as De Novo Q-Subs. And then as of today, the 510(k)s that were not covered in other priorities already, Q-Subs are now going to be. So all 510(k) submissions now are going to be-- Q-Sub submissions are going to be accepted for review as of today.

So if you've been waiting for that, go ahead and send them in. And so we're back to normal in the sense that we're now reviewing all types of applications, including all Q-Subs in OHT7. However, due to the continued elevated workload due to COVID, it's likely that these IVD Pre-Submissions will initially be reviewed under an extended timeline.

It's my expectation that you get assigned a reviewer for your Q-Sub They will in a matter of days or a week or two will be able to tell you the expected timeline for that Q-Sub review. So thank you for your patience up till now and as we try to get back to normal on all submissions and this especially for non-COVID submissions.

Second, a big announcement is that the FDA has now posted a memorandum of understanding signed by CDC, AdvaMed, ACLA, AMP, APHL, the CAP, the Council of State and Territorial Epidemiologists, the FDA and the National Independent Laboratory Association.

This MOU covers diagnostic surge testing capacity for public health emergencies. The CDC will collaborate with partners and use its existing relationships with our government agencies and stakeholders in the laboratory community to support external laboratory surge testing capacity during public health emergencies and emerging public health threats. The CDC will lead the development of a national clinical laboratory surge capacity plan drawing on lessons learned from past experiences. That includes COVID, including in response to emerging pathogen outbreaks with pandemic potential.

Convene teleconferences and meetings with partners to inform solutions for implementing clinical laboratory surge capacity in response to emerging pathogen outbreaks with pandemic potential, and in preparation for enduring public health emergencies.

Develop and implement tabletop and full-scale exercises to assess and evaluate partner roles and responsibilities for implementing clinical laboratory surge capacity. In collaborations with partners of this MOU, identify academic medical centers and/or a private clinical and commercial laboratories with national or regional presence and specific testing capacities and capacities to participate in the response.

Facilitate coordination with other relevant government agencies to appropriately plan and implement a clinical laboratory capacity and laboratory testing response, including facilitating the communication of evolving regulatory requirements or suspension thereof, as such regulatory developments relate to the expansion of laboratory capacity and laboratory test development and validation during a public health event response effort.

So that is good news that we have a fairly large stakeholder group now that's going to be focused on this. With that, I think we can go to the next portion of our Town Hall, which is to take a look at the questions that had been submitted prior to today's call.

CDR Kimberly Piermatteo: Great, thank you, Tim. We'll now answer your previously emailed questions about COVID test development and validation. Again, as we've mentioned before, please note we have received 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 that few days, please feel free to reach back out to CDRH-EUA-Templates@fda.hhs.gov mailbox for an update.

Kris, I'll be directing these questions to you. So our first question is, is FDA currently accepting EUA requests for multiplex antigen tests that can detect a combination of viruses such as SARS COVID-19 and influenza intended for use in a point-of-care or over-the-counter setting?

Kristian Roth: Yes. Thank you, Kim. So, yes, FDA has authorized several antigen multi-analyte diagnostic tests intended for use at laboratory and POC sites. We currently don't have any multi-analyte OTC tests authorized at this time. However, we have recommendations in the appropriate template. And these types of tests do meet the current priorities.

As we've noted before, if you are considering an OTC multi-analyte test we recommend you submit a pre-EUA to further discuss your test design and proposal.

CDR Kimberly Piermatteo: Thanks, Kris. Alright. Our next question is some recently authorized, at-home home antigen tests-- for example Xiamen and Osang include tables showing performance calculations at varying percentages of low positives. Can FDA clarify the PPA requirements for simulated models like these? And then the second part of that question is, can these same logic be applied across Flu A and B data for multi-analyte tests?

Kristian Roth: Yes, thanks. So data from recent prospective clinical studies with the Omicron variant have shown an unexpectedly high percentage of low viral load samples. We've seen ranges from about 30% to 40% with significantly poor performance with low positive samples compared to high positive samples.

Current performance targets are based on a target of 10% to 20% low positives in the clinical study. Where data sets that have more than 20% low positives, we have additional recommendations that can be used to calculate performance within the 10% to 20% target. However, there are caveats to this approach. And so far, it has only been used for SARS-CoV-2 tests, OTC antigen tests evaluated by the NIH as Independent Test Assessment Program which is called ITAP.

This program uses a study design developed in collaboration with us. These tests all have a similar test design. They use a calibrated RT-PCR comparator method. And there are other properties of these tests in this program which allow for this type of analysis.

So at this time, this approach is not appropriate for multi-analyte tests. And really, the approach should be discussed with us after your clinical study is performed and with confirmed Omicron positive samples. And if you have collected more than 20% low positives in your prospective clinical study, then please submit all of your data, including all the low positives. And we can work with you on this new analysis approach.

If you've not yet completed your clinical validation and are planning your approach, we recommend you submit a pre-EUA if you'd like to discuss your study design, including the percent of low positives and the comparator method. Again, this approach is only applicable to SARS-CoV-2 OTC antigen EUA tests.

CDR Kimberly Piermatteo: Thank you, Kris. Alright, our last previously emailed question is, we are currently conducting a prospective clinical study to support an at-home, rapid antigen test. One of the exclusion criteria recommended in the antigen template is -- Knows infected status (positive or negative) based on a predecessor COVID-19 test resulted in 14 days prior to enrollment. Is this exclusion criteria appropriate to apply to symptomatic subjects? If so, what should be considered a predecessor COVID-19 test?

Kristian Roth: The answer is yes. This inclusion criteria is appropriate for symptomatic subjects. And all COVID-19 diagnostic tests-- both antigen and molecular are considered predecessor tests. Currently, there are numerous tests available to many U.S. citizens. If you are observing that many individuals in your study have a known test result within the 14 days prior to enrollment, we recommend reaching out for additional recommendations specific for your clinical study design.

CDR Kimberly Piermatteo: Thank you, Kris. So that wraps up our previously submitted questions for today. We will now take your live questions. To ask a live question, please select the Raise Hand icon at the top of your Zoom screen. When you were called on, please follow the prompt and Zoom to unmute yourself. Then identify yourself and ask your question.

Please remember to limit yourself to asking one question only. If you have an additional question, you may raise your hand again to get back into the queue. And I will call on you if time permits. And please remember, we are not able to discuss specific submissions under review.

So our first live question for today is coming from Jennifer. Jennifer, I'm going to unmute you. Please unmute yourself and ask your question.

Jennifer Stanford: Thank you. This is Jennifer Stanford calling from Hopkins MedTech Compliance. And my question is regarding the multi-analyte test that we were just talking about. If we have a device that's looking at COVID as well as Flu A and Flu B, it's been addressed, I think, in the past that Flu B is not as common in the United States and that some studies might be able to be conducted outside of the U.S. So our question is, would we be able to conduct a trial, say in China or Columbia, another country?

Timothy Stenzel: My apologies. I was on mute. Is this an at-home test or a point-of-care test?

Jennifer Stanford: Well, it's an at-home test. Sorry. Over-the-counter at-home test. It's a multi-analyte.

Timothy Stenzel: OK. The challenge in some countries is we really need English and/or Hispanic speakers, and Chinese speakers aren't going to-- Chinese-only speakers aren't going to do for that.

And so yes, understand that going outside the U.S. is going to be-- may be necessary for Flu, particularly Flu B. I understand that in the Southern hemisphere, there has been a higher percentage of Flu B right now in the United States. Last I checked it was below 1% of flus in the U.S.

So we're open to that. I think before you take an at-home test to another country for testing, that you run that plan by the FDA in a pre-EUA just to make sure that the setting on the languages are covered. So one of the things that we've seen with at-home tests, even non-COVID tests in foreign countries, is that some sponsors think that they can provide instructions in, say, native language like Chinese in addition to the labeling that would go into the package in the U.S., which is English and/or Spanish primarily. And that's not acceptable to translate into another language. Because we're testing, really, in these studies that the labeling, as well as the tests, all works together in harmony and yields an acceptable result.

So testing another language that isn't going to be provided in the U.S. and isn't widely used in the U.S. is not going to be helpful-- so long-winded answer. But we're open to it if it's-- it's best to run it by us and focus on, I think primarily on our English speakers and readers outside the U.S. if you have to go that route.

Jennifer Stanford: Right, ok. And what is your thought on frozen Flu B samples if we were able to get some banked samples?

Timothy Stenzel: For molecular assays, we're going to have probably an easier time of that. Although, it's not a clear pathway. But banked samples for home is going to be a challenge no matter what. Because you're really testing on the ability of the device to detect.

And we have plenty of point-of-care flu devices in the United States and central lab tests. So a point-of-care is a little bit easier for molecular assays. But antigen assays are going to be a challenge. But the only way you can do this either frozen direct swab or frozen VTM primarily. And there are issues with each as far as-- we've seen sensitivity changes with a freeze thaw, particularly for antigen tests. And we've seen significant issues with transport media and antigen test performance, namely false positives with VTM. So, again, it's complicated. And I suggest a pre-EUA discussion with the FDA.

Jennifer Stanford: Great. Thank you so much.

CDR Kimberly Piermatteo: Thank you, Tim. Thank you, Jennifer for that question. Our next question is coming from Priska. Priska, I have unmuted your line. Please unmute yourself and ask your question.

[INAUDIBLE] Priska, we're having a very hard time hearing you. It's breaking up quite a bit. [INAUDIBLE]. It's still very-- it's still very choppy. And we're have a hard time understanding you. [INAUDIBLE]

OK, I think at this point, I'm going to go ahead and mute you again. And if you can get a better connection, please feel free to raise your hand again later, OK?

Alright, our next question is coming from Homer. Homer, I have unmuted your line. Please unmute yourself and ask your question.

Homer Wu: Hi, thanks for taking my call. I'm from Hopkins MedTech Compliance. We have a client, actually they developed an automated instrument which take the EUA-approved antigen test. They automate the sample piece like the buffer wash process. And they can read user camera and give a result. My question for this kind of instrument, do we need to apply for EUA or is there any other way we can to get approval for this kind of instrument?

Timothy Stenzel: Well the EUA path is open for you as well as the full authorization pathway, whatever you choose. It would be easier to get this added to this test at the moment more quickly using the EUA pathway.

Homer Wu: OK.

Timothy Stenzel: And so the best way is-- I don't know if the owner of the antigen test EUA is working with you with this process. That's going to be the easiest way to add this to that test. It's going to be a challenge if you're not working with the original owner/submitter of the EUA. Because it would be a modification of that EUA.

Homer Wu: OK, I guess my understanding is if we have developer for which has the EUA approved, if we work with them, if we get approved, then this instrument can only work with that EUA-approved test, right?

Timothy Stenzel: Yeah. So you're -- fully-supports automating anything that can be automated for the antigen test or any of the tests, including the interpretation. But that obviously, can change the

performance of the test. Because it's no longer a manual done process that's been tested in the past. And it's no longer a manual read. And we have some issues with instrument reads of antigen tests.

Homer Wu: OK. I understand. Alright, thank you.

Timothy Stenzel: You're welcome.

CDR Kimberly Piermatteo: Thank you, Homer. And thank you, Tim. Alright, our next question is coming from Rainer. Rainer I have unmuted your line. Please unmute yourself and ask your question.

Rainer Ziermann: Thank you. Can you hear me?

CDR Kimberly Piermatteo: Yes, we can.

Rainer Ziermann: Great. Thank you very much for taking my call. This is Rainer Ziermann. I just read yesterday the new information that came out. And I want to really thank the agency for the enormous work you're doing based on the number of submissions. I was quite stunned reading this.

I was wondering whether you can comment on the prioritization at this point in time of submissions for molecular point-of-care tests in regard to whether these are EUA submissions or 510(k) submissions? Does the agency prioritize one over the other? Because that, of course, is relevant for the development of these products. Thank you.

Timothy Stenzel: Yeah. So a COVID point-of-care and molecular test that meets the November 15th, 2021 guidance of volume minimums will be prioritized for EUA review. So if you meet those stipulations in that November 15th guidance, the EUA pathway continues to be the easiest pathway to get on to the U.S. market with a COVID test-- either COVID alone or COVID along with other viruses.

But the 510(k) pathway is open to you now that we have authorized-- we granted the first De Novo for molecular COVID tests and even a follow up 510(k). So you have your choice of either. The EUA is going to be a little bit more streamlined path to get onto the U.S. market. We do recommend, though, that the developers consider their long-term interests as far as whether they want to be on a market long-term.

And if that's true, that everybody begin working on their 510(k) submissions for molecular tests. And for antigen, the first submissions would be De Novos as well as for serology. Hopefully, that answers your question.

Rainer Ziermann: Yes, it was very clear. Thank you very much, appreciate it.

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

Ingrid Caton: Hi, good morning and good afternoon. Ingrid Caton from NOMAD Bioscience. I was just going to piggyback on the previous question on do you have guidance for multiple analyte molecular diagnostics for over-the-counter use? And is there clarification on the multi-analyte piece on the guidance documentation for either the De Novo or 510(k) submissions?

Timothy Stenzel: So the first test-- and I'm going to let Kris respond to this as well-- that we granted and then the subsequent 510(k), were multi-analyte devices. So you can look to those full authorizations, the grant, the special controls that go with it for our thinking a large part on a full submission for those kinds of tests. And then the door is open for Q-Subs, Q-Submissions, for full authorization. So you can use that pathway to ask questions and run study designs by the FDA.

Kris, do you want to add anything?

Kristian Roth: Sure. So you can look into the FDA De Novo database and look for the BioFire RP2 test. And that has a decision summary in there that has a lot of information related to how that test was validated, both analytically and clinically. And of course, those special controls do cover single-analyte and multi-analyte molecular tests. And that would be both in a high-complexity laboratory and then a moderate complex device.

And then if you're going to further extend the claims to CLIA waiver, then that would be kind of a typical CLIA waived approach that has been done numerous times. So we can discuss that in the context of a Q-Sub. Or there's also numerous decision summaries available for multiplex upper respiratory infection tests that have been CLIA waived as well.

Timothy Stenzel: And then as far-- I think you had, was it a potential home test? We do have guidance in our templates on a multi-analyte home test that you can look at. And then for a submission for a home molecular test, a full submission, then we haven't authorized one of those yet. So I would recommend the Q-Sub approach to address questions about your plans and whether they're going to be sufficient for that authorization.

Ingrid Caton: Yeah, thank you. I was focusing on over-the-counter piece. Appreciate that guidance.

CDR Kimberly Piermatteo: Alright. Thank you, Ingrid. Our next question is coming from Kal. Kal, I have unmuted your line. Please unmute yourself and ask your question.

Kal Mansoor: Hello. Thank you for taking my question. So based on two recent authorizations, we noticed that the overall PPA was 64.2% and 67.1%, which is lower than 80% PPA. So is this a signal that FDA is more open to lower performance and will this be captured in a template for everyone else to be aware of for the minimum performance requirement? And if so, can a similar approach be taken for a multi-analyte Flu A and Flu B test?

Timothy Stenzel: Yeah. So, Kal, thanks for that question. That was covered in pretty good detail at the top of the call. Because we had a pre-submitted question on this. So I'll just quickly recap. And then you can look to the transcript to get the more details on this.

No. This isn't lowering the bar. We see that with the Omicron it's a lot more of low positive and our template says for antigen, it says-- and this is only appropriate for antigen tests-- that we expect to see 10% to 20% antigen test positivity. And then when we're seeing 30% to 40% with the recent ITAP study that was above our expectations. So we modeled-- if you saw the normal previous 10% to 20% and your performance was at an 80% or above and the lower bound was greater than 70%-- was greater than or equal to 70%, then that was the acceptable performance for authorization.

We will not apply this to other viruses other than COVID. Kris, anything to add?

Kristian Roth: Nope. That covers it. Thanks.

Kal Mansoor: So can I ask a follow-up question to that. So does that mean that we cannot use this approach if we have a SARS-CoV-2 target in a multi-analyte?

Timothy Stenzel: Kris, are you prepared to be able to answer that today? What Kris did say ahead of time is to run your study. And then submit the data to us. And we'll take a look at the data. And we want to see all the data from the study, not just the first 10% to 20% positive. Kris, anything else?

Kristian Roth: No. I think so that would be new territory. And I think this call really want to go over items that have already been put out there. And so this is something new. And if this is an approach you want to use for multi-analyte test, and we're glad to address it in a pre-EUA or other written context.

Timothy Stenzel: And you can also do your study. And if you run into a problem seeing a high percentage of low positives for COVID, submit your data. And we'll look at the totality of evidence. We did do some additional special steps with the ITAP tests that we could do within that program.

And so it's going to be more difficult for developers who haven't gone through that program to mimic what we did there. But there are potential ways to do that. And we can either discuss that, as Kris said, in a pre-EUA. Or if you submit your data, we can have a discussion at that point.

Kal Mansoor: OK, thank you.

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

Wenli: Thank you. This is Wenli from XYZ Laboratory. Thank you for taking my call. And I have a question regarding what Tim just talked about-- the FDA and CDC'S effort for preparation for emergency response, such as increasing the lab testing capacity and other things.

My question is we are not developing a method which we believe can increase the lab test capacity and multiplex molecular method. So we are planning to submit the pre-EUA to the FDA. So my question is if this worked and is still valid, will still go this way to discuss our method and discuss our intention others?

Timothy Stenzel: Yeah. In an emergency situation, EUA statute applies. And that's the pathway to go. The CDC in conjunction with the labs look at how we can expand lab capacity, surge capacity, using the available tests that are regulatory allowed.

So it's two different things really. You have test developers. And then you have labs that are running the tests. And if you have a whole lot of tests, but you don't have the lab capacity that's needed, then that's a challenge. And so, really, the federal agencies work in concert here. The FDA focuses on authorizing tests. Our priorities now are on high-volume tests. And the CDC'S focus, among other things, is to make sure that the labs have what they need as far as being able to do those tests.

Wenli: OK. Yeah. OK, got it. So we can still just do the regular way to apply for--

Timothy Stenzel: Yeah. This does not change in any way-- in any way, the EUA statute. This is designed to engage the lab community in planning and execution prior to and during emergencies, to deal with the totality of the needs for the country.

Wenli: OK. Thank you.

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

Andy Wang: Thanks for taking my call. This is Andy from-- Andy Wang from PGIE. I have a follow-up question around the previous question. Regarding this emerging virus bacteria infections, such as monkeypox, and how do we enable the local labs adopting PCR tests, home-brewed or CDC type of test doing their own validation as there are no or very rare positive cases patient samples?

Timothy Stenzel: Yeah. So for the volumes that we're seeing right now for monkeypox in the United States, the CDC and the Association-- the Public Health Lab members of the Association for Public Health Labs, there are, I believe, 67 state and local public health labs that have the FDA-cleared CDC assay.

And the laboratory testing capacity within that public health lab network greatly exceeds the current cases of monkeypox in the United States. At least at the moment, there does not appear to be a need today for a lot more testing capacity.

That said, I do want to cover monkeypox in a little bit of detail today. So the availability of emergency use authorization for COVID-19 tests is available due to the Secretary's declaration under Section 564 of the Federal Food, Drug, and Cosmetic Act of emergency or threats justifying authorization of emergency use for a product. For tests for viruses that do not have an act of emergency declaration under the Food, Drug, and Cosmetic Act, traditional review pathways-- De Novo, 510(k), PMA are available.

The CDC already have, as I said, an FDA-cleared assay for non-variola Orthopox, which detects monkeypox. And since it's the only non-variola Orthopox circulating in the U.S. potentially right now, that test is perfectly functional to detect any monkeypox cases. And the public health labs know that they can act on those positive results.

And there may also be laboratory-developed tests available for Orthopox or specifically for monkeypox, LDTs or Laboratory Developed Tests are tests develop use within a single high complexity CLIA-certified laboratory. The FDA has generally exercised enforcement discretion for LDTs, meaning that the agency generally does not exercise its authority to enforce the regulatory requirements for these devices. Although, it maintains that authority.

The general enforcement discretion policy for LDTs has not applied in limited circumstances, including tests used during declared emergency under the Food, Drug, and Cosmetic Act. In the case of an emergency involving an outbreak, inaccurate tests can lead to greater spread of the disease and poor management of the outbreak due to false results.

FDA has, therefore, expected emergency use authorization for LDTs during all prior declared emergencies, including the H1N1 in 2009 and continuing through the current COVID-19 emergency. The FDA is preparing a molecular template for potential use if an emergency were to be declared for

monkeypox under the Food, Drug, and Cosmetic Act. We will also monitor the situation with respect to appropriate policies for tests in the event of a declared emergency.

I'm not saying, however, that there is going to be an emergency. So right now, monkeypox, Orthopox is covered under enforcement discretion for LDTs.

Andy Wang: Great, thanks.

CDR Kimberly Piermatteo: Thanks Tim for that. At this time, I'd like to go ahead and make a call out if anyone else has any questions they would like to ask Tim or Kris today, our panelists today. Please let me know. Raise your hand.

OK. I am seeing none additional raised hands at this time. Wait one second. We have a raised hand from Wenli. Wenli, I'm going to go ahead and unmute your line. And you may ask your question.

Wenli: Thank you. This is Wenli again. And I have some thoughts. And I'd like to get your comments. So we are doing this as a laboratory-- we're doing this comparator test using the EUA test, molecular EUA assay, right? And many of those EUA assays, they develop an assay. But in terms of the sample shipping condition or handling condition or the VTM or whatever, those things, they use the CDC general guidelines-- the VTM requirement and also shipping and handling storage requirements.

Those general guidelines, we found that we have done a lot of internal test and experiment. And the study shows that actually SARS-CoV-2, they're pretty stable, very stable. However, the general guideline at CDC said or 72 hours, within 72 hours, it only stayed at 4 to 8 degree for 72 hours then you have to deep freeze them, the samples.

But in the laboratory situation, once the sample's here, even overnight where we do the test, even on the same day, then you still need to give a couple of days for potential repeats and retests. It's easy to exceed 72 hours. And then if you strictly follow the protocol of those EUA IFU, they have to freeze the sample and then thaw them.

This actually sometimes may be detrimental. So I think my thought here is that whether the FDA would accept-- say, if a lab, I have a very well-documented validation on the storage condition and for the medium-- for the specific VTM or the other medium, then this is acceptable so we have to extend the time a little longer to be able to process them.

So this is just some of my stuff. Right now for the EUA, it's OK. Because the sample-- the number of comparators are not that large. But if we think in the future, like some company, they want to go to the 510(k), there was supplement by testing many, many more samples, then it's really difficult to finish everything on the same day we receive the sample. That's what we're I'm thinking ahead to see what is FDA'S flexibility on this regard?

Timothy Stenzel: So the FDA has authorized EUA tests and/or grants or 510(k)s with information about a sample transport and sample stability. And if the test has been validated only out to 72 hours at 2 to 8 degrees, we don't know the stability of the samples beyond that.

And so if you have any discrepancies in your study because of say delayed testing, that should be noted on the line listings for that patient and that testing. If you have questions about this, if it's a very

frequent occurrence, you can engage the FDA either, if you were already working with a reviewer, for the reviewer, or in a pre-EUA to ask what to do in that situation.

Certainly, additional studies could be done to show sample stability for a given EUA. But that's something that we hope doesn't have to be done. Kris, do you have anything else to add concerning that question and my answer?

Kristian Roth: No, I don't. Thanks.

Wenli: Yes. So basically, as a lab, we cannot really supplement with the stability test done on our own to show that to activate that, for example, the storage condition and others can be—

Timothy Stenzel: Yeah. This is a very specific question. So if you do have an issue with not being able to turn around the sample in the time specified in the instructions for use in the EUA or fully authorized test, then I would engage the FDA and what to do in those cases.

Wenli: Yeah. So for [INAUDIBLE] sample, there's no problem. They ship on dry ice. There's never been a problem. It's just for some shipment they sent to use the ice. And that is—

Timothy Stenzel: I understand.

Wenli: Yeah.

Timothy Stenzel: I understand. And frozen samples should be allowed for these studies as well in the EUA authorization. So if you're using frozen samples where the EUA test does not validate and report use of frozen samples then that's another item that we'll want to know about in your licensing. But it's best to talk about it before you submit that data to see if any of that's going to be acceptable. Alright, I think we have a few more questions.

Wenli: Alright, thank you.

CDR Kimberly Piermatteo: OK. Thank you. Alright, our next question is coming from Michaela. Michaela, I or Michaela, I apologize. I have unmuted your line. Please unmute yourself and ask your question.

Michaela Hoffmeyer: Yes, hi. This is Michaela Hoffmeyer with TE Connectivities IVD Solutions Group. We're a clinical research organization. So there have been a couple of questions today. And it sounds like the agency is clarifying for antigen tests, that PPA target of 80% given that recent clinical studies are showing low positives approaching more of the 30% to 40% as opposed to the 10% to 20%.

So my question is really simple. I just want does that rethinking of the performance, is that applicable to just antigen OTC tests? Or is that something that we can engage the agency in a discussion with for an antigen point-of-care test as well? Thank you.

Timothy Stenzel: Yeah. You can engage us on that. I mean, it's really our current thinking around antigen tests. So the current template, which has been in place with recommendations for antigen test validation called for there to be 10% to 20% of low positives at a minimum. And we were, up until about January 1 of this year, that was typically what we were seeing in submissions.

Sometimes, we didn't see it. And that was a potential red flag if we didn't see low positive. But when we began seeing more and more, significantly more low positives and that directly degraded the overall PPA, it's just we hypothesized that this is a behavior of the virus with Omicron and potentially contributing to lower sensitivity of antigen tests in Omicron.

But it would be unfair to hold tests that are being validated in the Omicron era to not take that into account. Because potentially, any previous tests-- had it been validated during this time period, might suffer from the same challenges that we're seeing with these tests.

One thing that we do do in the ITAP program is we do make very careful analytical comparisons, analytical sensitivity comparisons between candidate tests and prior authorized tests as a measure of relative sensitivity. So we do know that these candidate devices are at least as sensitive as some other EUA-authorized tests at the bench level.

We also know that some candidate devices on Omicron pools within the ITAP program are falling less sensitive than some of the previously authorized tests. And so that is a challenge for those developers of those tests. Because we are trying to hold the line on overall sensitivity so that these antigen tests continue to-- they're authorized to continue to perform relative to each other, relatively-equally well.

Michaela Hoffmeyer: Thank you very much.

Timothy Stenzel: You're welcome.

CDR Kimberly Piermatteo: Thank you. We have time for one more question. That question is coming from Sue. Sue, I have unmuted your line. Please unmute yourself and ask your question.

Suehibbein: Hi, Thanks for taking my question. I just wanted to ask about some rumors that I've been hearing through other people in the field and people involved in RadX programs that I keep hearing that FDA is going to stop accepting new EUAs as soon as the next couple of weeks.

And so I was just wondering if you could talk a bit about that. And I apologize. I missed a little bit of the beginning. So I don't know if you talked about this already.

Timothy Stenzel: No, the current guidance is that we're accepting EUAs under the policy established on November 15th, 2021. And nothing has changed as a result of that. We are trying to get back to normal. I don't know when and if any changes will occur.

Suehibbein: OK. So not in the next couple of weeks?

Timothy Stenzel: So I can't make any promises. We have authorized over 470 tests. We have a number of tests still in the pipeline that could very well be authorized. That's the current situation. We have 20 OTC tests authorized. We have huge manufacturing capacity. We have an overabundance of home tests now in the United States as today. I can't predict what it will be tomorrow. Those are just the facts. And I can't predict when the need for these tests will go away.

Suehibbein: Thank you.

CDR Kimberly Piermatteo: Great. Thank you, Sue. And thank you to Tim and Kris. We appreciate everyone's participation today.

As I mentioned earlier, a recording of today's Town Hall and transcript will be made available on CDRH Learn. Please visit CDRH Learn at the link provided on this slide. You will find a 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, you may send an email to CDRH-EUA-Templates@fda.hhs.gov.

And lastly, please remember to join us for the next IVD Town Hall scheduled on Wednesday, June 15th, 2022 from 12:05 to 1:00 PM Eastern Time. Again, thank you for joining us today. And this concludes our Town Hall. Have a nice day.

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