Virtual Town Hall #78
February 9, 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 78 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 titled Coronavirus, COVID-19, Test Development and Validation Virtual Town Hall Series. The January 12th Town Hall recording and transcript are posted and we hope to post the January 26 recording and transcript by the end of this week. The next scheduled IVD Town Hall will take place Wednesday, February 23, 2022.

Our panelists for today's program are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health, or OIR, in CDRH's Office of Product Evaluation and Quality; Toby Lowe, Associate Director for Regulatory Programs in OIR; and Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices, also in OIR.

We are going to start off with answering your previously emailed questions to us. Please note, we receive some questions that are too detailed or test case specific, and we will not be able to address them on this call. 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, please look for a written response. If you do not receive one within a few days, please feel free to reach back out to the CDRH-EUA-Templates@fda.hhs.gov mailbox for an update. And then, after we have completed going through your emailed questions, we will open the lines up for your live questions. So let's get started with the first email question.

So the question has come in. What is the time frame for HHS, Human Health and Services, withdrawing the public health emergency for COVID-19, and what is the FDA's current thinking on the IVD transition plan?

Toby Lowe: Thanks, Joe. So we can't anticipate when the public health emergency will end. Um we have mentioned previously here on this Town Hall both that we don't know when the emergency will end, and that we are working on a transition plan for devices that are offered under EUA. In December, FDA issued the draft guidance "Transition Plan for Medical Devices Issued EUAs During the COVID-19 Public Health Emergency," and that is a draft guidance issued for comment. That can be found on our website.

Since it is a draft guidance that's been issued for comment, not for implementation, if there are points about the guidance that are unclear, we recommend that you submit a comment to the docket, indicating areas that could benefit from additional clarity. If you have questions specifically about how to manage your current plans for moving forward now with your emergency use test or with a 510(k) please send an email to the EUA templates mailbox with sufficient details about your specific situation and your specific test so that we can provide appropriate feedback.

Additionally, unless revoked, EUAs are in effect until the public health emergency is terminated. This, in previous public health emergencies, has not happened for quite a while, as can be seen by the previous public health emergencies that still have not been terminated, such as Zika and Ebola. And it's important also to note that we have already granted a De Novo and cleared a 510(k) for COVID-19 molecular tests. And we do welcome additional 510(k) case submissions for molecular tests.

We have not yet granted full marketing authorization for antigen or serology tests, but we are interested in doing so, and a De Novo would be the first step for each of those.

Joseph Tartal: Thank you, Toby, for that comprehensive answer. For this next question, I'll turn to Tim. If a developer of an over-the-counter antigen test submits clinical data in an emergency use authorization that predates omicron and delta, what specific testing for omicron and delta does the test developer need to submit?

Timothy Stenzel: Yes so we are not asking for any delta specific data. We are asking for omicron data, though, as the FDA variant mutation website says that there could be decreased sensitivity for omicron. And we're wanting to establish performance with omicron, since it's essentially 100% omicron now. Whether the application is currently under review or it's a new application, at this time we do want to see omicron data prior to making our authorization decisions.

Let me go into a little bit more detail about what we're looking for here. Talk to your lead reviewer if you've already submitted something. Or you can ask the question in a new submission about what to do. But there are two different pathways that could be utilized here. One is that, since omicron is circulating right now, if you add new clinical study data during a time when omicron is essentially dominant that is good evidence of what the performance will be for omicron. If your application is already in-house, we may decide if the data looks good, that that sequence confirmation can await a post-market commitment. But if you're going forward now, we would like to see sequence data. If you haven't started your study or now, I would like to see sequence data in the application showing that the sample is omicron so we know how to establish performance with omicron because we know which samples are omicron.

As regards to what sequencing procedure to use, check with the FDA on that one. There are a couple of EUA authorized sequence assays, but, in general, as long as it's a validated sequence as a whole genome sequence assay with good performance, and you can show that to the FDA, that should be sufficient for confirmation that the sample is omicron.

There's an alternate pathway. If you should happen to have banked dry swabs for omicron, or even swabs collected only in saline, we can consider this. For those that have applications before the FDA right now, we would ask that a minimum of 10 samples that represent omicron be submitted for our review prior to authorization. I think that's pretty extensive feedback on that, so we'll let that go for now with that. Thanks.

Joseph Tartal: Thank you, Tim. So our next question, the antigen diagnostic template states that VTM, viral transport media, should not be used as a dilutant for analytical studies if it is not indicated for use. Can PBS, phosphate buffered saline, or saline be used? Toby?

Toby Lowe: Thanks. Yes, VTM should not be used in any analytical validation studies if it is not indicated for use with your test. And PBS or saline can be used as the dilutant used to create negative clinical matrix with patient negative samples.

Joseph Tartal: Thank you. Going on to our next email question. The revised policy for coronavirus disease 2019 tests during the public health emergency, revised in November, guidance states that FDA is prioritizing laboratory-based and point of care serology tests that are intended for the quantitative detection of neutralizing antibodies. What is FDA's current thinking about these tests now, given the prevalence of omicron? Is FDA requiring tests to detect antibodies that are specific to the omicron variant?

Toby Lowe: Thanks, Joe. Similar to developers of other COVID-19 related tests, developers of neutralizing antibody tests should monitor new and emerging viral mutations and variants, such as omicron, on an ongoing basis and assess the potential impact on test performance. In their EUA request, we would want to see information on the potential impact of the mutations and variants on test performance, or an explanation of how the risks associated with unknown performance in samples from individuals infected with the variants can be adequately mitigated.

For more information regarding evaluating the impact of viral mutations and variants, you can take a look at the policy for evaluating impact of viral mutations on COVID-19 tests, which is available on our website, as well as the template that is specifically for serology tests that detect or correlate to neutralizing antibodies. The current version of that is dated October 6, 2021, and is also available on our website.

Timothy Stenzel: And I would just clarify that the FDA is not asking for serology tests that can detect antibodies raised to omicron. Thank you.

Joseph Tartal: Thank you Toby, thank you Tim. It looks like this next question will be for Tim. During the last Town Hall meeting, Dr. Tim Stenzel said that positive samples in the clinical study of antigen rapid tests need to provide sequencing variant info. Can FDA provide recommendations on authorize validated sequencing tests that should be used to determine sequencing data? Are all clinical positive samples used to validate an antigen test required to be sequenced, or can we do a subset?

Timothy Stenzel: I pretty much answered this question already. I would just further clarify that we want to see sequence data eventually for the entire set that you're presenting to us. Thank you. That'll be all on that.

Joseph Tartal: Thank you, Tim. So now we're going to move on to our live questions. Please raise your hand. We already have some hands raised. What I'm going to do is I'm going to announce your name, I'm going to unmute you, then you need to unmute yourself, and then ask your question promptly.

When I unmute you, please provide your identification, your name, and then ask your question. We do ask that you only do one question at a time. Once that question is answered, if you want to get back in the line, that's completely acceptable. We do want to get to as many different people as possible. And again, just like with regards to the email questions, we can't talk about any specifics as it relates to an authorization or a submission, so please keep those questions as broad as you possibly can.

With that, we're going to go on to our first live question. Andy Papon, I'm going to unmute you, please unmute yourself and ask your question. Ok, not hearing anything, therefore we'll move to our next question. Richard I'm going to unmute yourself. Please unmute yourself and ask your question.

Richard Montagna: Thank you for taking the call. This is Richard Montagna from Rheonix. I know that the FDA is not able to respond to specific questions about a specific submission, so I'll try to frame this in a very general way. We submitted an amendment to our PCR EUA back in September. It was intended to validate the assay as a moderate complexity rather than the originally authorized high complexity. We were notified that it was in the triage, it would be evaluated, but for the past five months, we've got nothing but the biweekly updates. I'm wondering, is this what we should expect, or is it possible it's fallen through the cracks? Because it's also impacting another amendment we want to send in that will reduce the time of the assay. And we don't know whether we should run that with the software that would be used for high complexity or whether we should run it with the moderate complexity, because we don't know where we stand on that. I guess the question is, is it possible that it fell through the cracks, or is this what we should expect? So thanks for any guidance.

Timothy Stenzel: Sorry for that experience. If you just follow up later today with an email to our templates email inbox and relay this information and ask for Tim and Toby to be copied, I'll go ahead and figure out what's going on and get a response back to you.

Richard Montagna: OK, thank you very much. I really appreciate it.

Joseph Tartal: OK, thank you our next question, Karl. Karl, I'm unmuting you. Please unmute yourself and ask your question.

Karl Enters: Hi, Karl Enters, Vice President of Regulatory Affairs at GENETWORx. We have a situation where we have a bunch of high complexity labs coming to us, looking to have us do some overflow testing at the height of these peaks. The interesting part is, we use a nomenclature submitted in all of our EUAs for the test reporting as positive, negative, and invalid. These requests are coming in with result reporting language on the client basis as detected, not detected, and tests not performed. And they'd like us to comply with that. What GENETWORx is proposing is that we would not change anything with our existing business or any of our systems, but just create a secondary shell reporting matrix to convert our results to their preferred language. Is that acceptable to the FDA?

Timothy Stenzel: That's a pretty specific question, so I would ask that you direct that to the templates email box and ask for it to be referred to Toby and Tim, and we'll get a specific response back to you.

Karl Enters: All right, thanks so much.

Joseph Tartal: OK. We'll go to our next question. Homer, I'm going to unmute you. Please ask your question. Again, please keep all questions as general as possible. For anything that is very device specific, you can email the device's email box at CDRH-EUA-Templates@fda.hhs.gov. Homer, you're unmuted, please unmute yourself and ask your question.

Homer Wu: Yes I think I'm unmuted. First, thank you for taking my call. My name is Homer Wu, I'm from Hopkins MedTech Compliance. We are actually helping a couple of manufacturers to run their clinical evaluation study here. Since now, omicron dropped so quickly, a lot of our sites the positive rate is so low, it's probably like 5%. I'm just trying to figure out, can we do some enrichment? For example, we

have a couple of sites, they actually run the tests, the standard kit test. But their results won't come up until the next day. And they actually don't say the results. Actually, the patients come back. So can we actually enroll those patients before we give them the results? And the purpose is to target those positive ones.

Timothy Stenzel: OK, thank you. Is this an at-home test, or is this a point of care test?

Homer Wu: Yes, antigen OTC. I'm sorry.

Timothy Stenzel: OK, so with all enrichment procedures, we do ask that the test developer firm reach out to the FDA and review the enrichment protocol so that any bias is avoided. One of the biases is knowing the results of a comparator test at the time that they are testing.

The other potential bias is introduced if a health care collection, a swab collection, is performed prior to the patient doing the self-collection and sampling. And so we just want to understand all those potential biases, control them in an acceptable way. And it's best before doing such procedures to check with the FDA review staff. Because we have, in some cases, unfortunately, firms didn't do that and they introduced unacceptable bias. And we were, therefore, not able to use the data. And that's a shame. So yes, understand that in some areas, omicron has fallen to very low levels or much lower levels than before. 5% is maybe still a little high to my liking from a public health standpoint, but I understand it does introduce additional challenges to getting the 30 positives that we asked for in the testing. Hope that's helpful, thank you.

Homer Wu: I'm sorry, we don't have a reviewer yet. So we haven’t submitted. So how are we going to follow up on this particular situation? Like the patients don't know the results yet.

Timothy Stenzel: Yeah, so we would like to review your study protocol, since it would involve enrichment. So you can submit that protocol as a pre-EUA to the template's email inbox.

Homer Wu: All right, OK, thank you.

Timothy Stenzel: Mm-hmm.

Joseph Tartal: Thank you, Homer. And our next question, Serdardemirel. I'm unmuting you. Please unmute yourself and ask your question.

Serdardemirel: Hello, this is Serdard from Antwerp Novatek Manufacturer. I have a very specific general question for you. How obligatory is the location of the usability study? You are writing that the usability study should be conducted in the USA. Can a usability study conducted abroad also be accepted provided that it meets the FDA's requirements?

Timothy Stenzel: We are recommending that US patients, consumers, laboratory and/or point-of-care workers be used in studies so that language, culture, workflow, and the types of settings that the tests are going to be used in the United States are assessed. So if you want to do something different than that recommendation, then I would suggest a pre-EUA with your protocols that have been used or would be used for FDA review and concurrence. That would be my recommendation before you start a study in case it's not acceptable once it gets to the FDA. So it'd mitigate your risk of that happening.

Serdardemirel: So we have submitted our application two days ago with a usability study conducted outside of the USA. It was conducted in the European Economic area. So we will await your answer. And thank you very much for your answer.

Timothy Stenzel: Yeah, once you get contacted by-- when your reviewer is assigned if they haven't been assigned already-- once you get contacted by a reviewer, then I would immediately ask that question, OK?

Timothy Stenzel: Thank you so much. Thank you so much.

Joseph Tartal: OK, thank you. Our next question is from Judy. Judy, I am unmuting your mic. Please unmute yourself and ask your question.

Jody Schulz: Hi there, this is Jody Schulz with Thermo Fisher. Thank you for taking my question. We have an EUA that has already been authorized for a PCR test. And I am curious from a high-level perspective if we are looking to change the software threshold for one of the controls if reanalysis of clinical data would be an acceptable form of verification testing without the need for additional clinical wet testing.

Timothy Stenzel: So this would just be for the controls?

Jody Schulz: Yes.

Timothy Stenzel: OK, I think we'd want to understand the motivation for that and any impact on the assay. And it's possible that looking at that depending on the assay design and how results are generated that that could be for a control part of the assay. That could be acceptable.

So I would suggest you send a pre-EUA in referencing the current EUA and explaining the situation providing enough background so the FDA can weigh in on your question.

Jody Schulz: Thank you.

Timothy Stenzel: Mm-hmm.

Joseph Tartal: OK, thank you, Jody. We'll go on to our next question, Mahesh. Mahesh, I am opening up your mic. Please unmute yourself and ask your question.

OK, I'm going to move on to our next question, Tian Yang, I'm going to open up your mic. Please unmute yourself and ask your question.

Tianyang Liu: Hi, thank you. So my question is that I know that for all of the EUA authorizations, the initial shelf-life will be most of them will be six months. But there are some icon flags at the initial shelf-life is 12 months. Could you explain how could we get a longer initial shelf-life?

Timothy Stenzel: So for antigen tests, we're giving an initial six-month expiration date based on accelerated studies only. If you have real-time studies that go beyond six months, then we can evaluate those at the time of submission. And then any extension beyond the original expiration dating provided will be based on the submission of real-time stability data to the FDA review and authorization.

Tianyang Liu: So you mean that if we have a longer time, for example, we have this product to sell in other markets other countries then it will be counted, right?

Timothy Stenzel: If the test is exactly the same as what is submitted to the US, and the quality control measures for stability testing are acceptable to the FDA, yes. Then longer period based on ex-US distribution is acceptable for FDA review.

Tianyang Liu: OK, OK, got it. Thank you very much.

Joseph Tartal: OK, thank you. Our next question is from Ho-Jun. I'm opening up your line. Please unmute yourself and ask your question.

Ho-Jun Suk: Thank you so much. So I have a quick question about the comparative method for molecular point-of-care test that we're developing. So the comparator that we are using has four possible result outcomes, which are positive, negative, invalid, and presumptive positives. And I believe the FDA has previously mentioned that presumptive positives should be considered as positives. But we were wondering if these presumptive positives have CT values that are beyond the stated LOD for the comparator if they are still considered to be true-positives for the purpose of clinical evaluation, or if they can be grouped into another group of result-type as a presumptive positive or possibly inconclusive, or if they have to be still considered as true-positive? If there's anything we can do, for example, sequencing or other methods to prove that these were actually just late false-positive amplifications from the PCR test, thank you.

Timothy Stenzel: Uh-huh, I'll initiate this and then Kris or Toby may have additional comments or sometimes, corrections when I get it wrong. But the first thing is that we do recommend that you use a high-sensitivity central lab molecular assay that provides CT results. We also recommend that you check with the FDA to make sure that the comparator test is acceptable. I'm not aware of a test that provides the output that you're describing among our authorized central lab molecular tests. But Kris or Toby may have additional details. But if so, it's an EUA-authorized test and it has these outputs. I think asking a specific question through a pre-EUA, or if you already have a submission to your lead reviewer is the best way to address this question. But I'll turn it over to Toby or Kris if they have any additional information or comments to add.

Toby Lowe: Yeah, no, nothing additional from me that covers my thoughts, Kris?

Kristian Roth: Yeah, I think maybe at first we had some presumptive positives tests or tests that had presumptive positive results but I believe we've addressed them. So I think we can discuss this in a pre-EUA so we know exactly the situation that you're describing. And we can help you pretty quickly, thanks.

Ho-Jun Suk: Got it. So to be on the same page, you're saying, to your knowledge that the lab-based, highly sensitive RT-PCR tests that can be used as a comparator for new molecular tests they shouldn't have presumptive positive as a possible result outcome. Is that the correct understanding?

Kristian Roth: That's our current, preferred status. There's hundreds of tests out there. So maybe one still has a presumptive result that hasn't been addressed yet. But I think our preference right now would be to get rid of that presumptive result. For instance, in one case, there was an E-gene target that had some cross-reactivity with SARS 1. And so, at first, there was a question, well gosh, what if there is SARS 1 circulating with SARS 2? Clearly, that question has been answered. There is no circulating SARS 1.

So that particular assay was addressed with regard to presumptive. I'm not sure of the exact case you're talking about. But again, we can discuss this within the context of pre-EUA and give you more detailed feedback.

Ho-Jun Suk: Got it, thank you.

Timothy Stenzel: I think that's the best advice. You know because if something's presumptive positive cause it may not be as specific that may not be a good comparator assay for you. You end up making your point-of-care tests look worse if that's potentially a false-positive. So it's all dependent on the specific test that you're looking at and what we know about that test. And it's why we frequently recommend that developers check with us before they select a comparator test to use in their studies.

Joseph Tartal: OK, thank you all. And we're going to move on to our next question. Steve, I'm unmuting your mic. So please, unmute yourself and ask your question.

Steve Wray: Thank you very much. My name is Steve Wray. I'm from Micropoint Bioscience and the question I have is, first of all, I want to thank you guys for all of your hard work and dedication over the last couple of years this has been a long road for all of us. So and hopefully, we'll see the light at the end of the tunnel.

And the question I have is related to that. And for those of us that are in process of still developing new, over-the-counter and waived antigen-type tests, can you give us an indication of how many tests are currently in the queue for authorization and what kind of your estimated review time may be?

Timothy Stenzel: Yeah, so that information-- first of all, thank you for your kind words and for your wishes that this pandemic will come to an end soon. I keep on hoping. So you know we don't give those kinds of numbers out. We endeavor to review applications as soon as possible. And those applications that come in, and there's no questions, right? Everything's laid out correctly and accurately and easily understood and read and follow the FDA recommendations on all accounts or checked in with the FDA if they wanted to change anything before doing their studies. And so we preset what's acceptable for the particular developer.

Then those applications go through very quickly. Anything that has any significant questions does slow down the review. And so the reviewers have to prepare responses and questions. And then the firms need to receive that and respond to those questions. And the FDA reviewers have to look at those responses and see if they're acceptable.

So those kind of back-and-forths after submission does have a tendency to significantly delay our review times for them. But, for example, you know we've now got the ITAP program. And because everything's laid out crystal clear in the ITAP program about how things are done, you know when we get a submission through the ITAP program, all those things have been preset. And we make our decision within hours of receipt of the final bit of data from the ITAP program. So and other developers can do the same thing if they follow the recommendations of the FDA and/or preclear any changes, thank you.

Steve Wray: Thank you, Timothy. You guys have done an outstanding job with your templates and then adjusting those templates where you've received additional information where necessary edits have been required. So as developers, we really appreciate that guidance.

Timothy Stenzel: You're welcome, thanks.

Joseph Tartal: Thank you, Steve. And for our next question, Paolo. Paolo, I'm opening up your mic. Please, unmute yourself and ask your question.

Paolo Mita: Hello, my name is Paolo Mita. I'm working at PRL, Pandemic Response Lab, in New York. My question really on serology tests. So we're trying to develop some serology tests for SARS-CoV-2. And um, my question is if you guys can shed more light or some word about the thoughts and prioritization of the FDA for the different serology tests, in particular, between a test to quantify antibodies against SARS-CoV-2 versus neutralization assay. Is there basically prioritization for review once submitted, basically?

Timothy Stenzel: Yeah, if you see our November 15, 2021 policy guidance update for SARS-CoV-2 tests, we're currently only prioritizing new, fully quantitative serology assays that are linked to the International Standards and report out in IU's and neutralizing antibody tests. So those are really the only new serology tests that we're reviewing. And then there also are volume requirements for those tests. So that's all specifically laid out in the guidance.

Paolo Mita: Yes, and sorry for this follow-up. So the WHO on International Neutralization-- sorry, comparator collaborators-- those are not applicable for omicron anymore. So did this change FDA view on this test, or the plans are the same?

Timothy Stenzel: So yeah, we really don't know the impact of the different variants. And so the WHO standard, we believe, still can apply for fully quantitative. We do ask developers, as mentioned earlier on the call by Toby, that all developers take a look at our variant mutation guidance. And that they assess their test at the time of development and submission in the future after authorization for impacts by the various tests. But fortunately, you know serology tests since infection generates polyclonal antibodies, that we haven't seen any specific signals to differences by variant or mutation. It could happen. But so far, it hasn't.

So you know do check with the pre-EUA's serology team on recommendations for assay design such as what antigen you use in your assay to measure development of antibodies. But obviously, with as many mutations that are occurring, as many new variants that we've seen that either will come along or past variants will recirculate or additional mutations will occur with an omicron to keep it the dominant variant circulating. You know switching serology tests based on specific viral variants you know could introduce a variability that may not be helpful. So you know we would like to hear your specific thinking through a pre-EUA on your serology test. And our team can give you specifics of that.

Paolo Mita: Right, thank you.

Joseph Tartal: OK, let's move on to our next question, Siamak. Siamak, I'm unmuting you. Please, unmute yourself and ask your question.

Siamak Tonekaboni: Hello, I'm working with iSTOC. It's a Finnish health care company. So my question is if you can explain what is needed to add an app to authorize OTC COVID tests in the following situation. In scenario one, if the app is for the purpose of providing the instructions for running the test and interpreting the test results, the same information provided in the quick reference guide, in addition, the app would be able to take a picture of the test only for the purpose of recording the results. And in

scenario B, when the same function as above, but the app rather than the user would interpret the results.

Timothy Stenzel: So an app that provides instructions is oftentimes helpful and would be in addition to the recommended physical instructions that come with a kit cause not all users have access to electronic communications or this app. So to be used in addition to an acceptable hard copy that comes with the kit.

Siamak Tonekaboni: Yes.

Timothy Stenzel: That's fine. It's recommended that the firm that developed or is developing the test be involved as it will be specific for their test. And then, as far as snapping a picture and interpreting the test results, again, those are features that the FDA is open to and I believe has authorized already. And again, it would be for development with a specific test. Along with that test developer, we will want to see how the application that reads the result independently verify its performance. And so if you're giving the users of that test the option of manually reading or reading through the app, we would want to understand the performance independently of a manual read. So that does involve more work. I would recommend that you send a pre-EUA if you look at our instructions for app development in the templates, and you still have questions, or you want to alter the recommendations we have. And in that, we would want to understand if you're snapping a picture and not interpreting the test what would be the purpose of snapping that picture? But Kris, Toby any other comments on this?

Siamak Tonekaboni: Thank you. My specific question is what studies is needed in these two case scenarios?

Timothy Stenzel: OK, I would refer you to the templates. And if you have additional questions, then submit those questions as a pre-EUA to the template's email box.

Siamak Tonekaboni: That's great, thank you.

Joseph Tartal: OK, let's move on to our next question. Alex, I'm unmuting your line. Please, unmute yourself and ask your question.

Alex Weinberg: Hello, this is Alex Weinberg with UserWise Consulting. Thanks so much for taking my question. The question is, for an OTC antigen test kit, the templates asking for 30 children to be enrolled between both usability studies and the clinical study. However, if we can make the argument of substantial similarity to an existing test kit on the market, would that reduce the number of children that we should enroll in the clinical evaluation study?

Timothy Stenzel: So that's a very specific question. And it's best handled via an email to our templates email box in a pre-EUA. And if anybody has asked a question and sent it, and we haven't already mentioned it during the prepared question and response segment of this call, we are planning to send an email response. So and that should happen within a few days of this call. And if it doesn't, you could reach back out to the templates email box and check with us.

Alex Weinberg: OK, thank you.

Joseph Tartal: OK, our next question is from Gail. Gail, I'm unmuting your line. Please unmute yourself and ask your question.

Gail Javitt: Thank you. This is Gail Javitt from Hyman, Phelps, McNamara. In the November 15 guidance, with regard to prioritization of serology tests, what is the definition of high throughput? It's provided for molecular but not for serology. And I want a sense of what that would mean, practically speaking for a serology test.

Timothy Stenzel: Toby can you respond to this one?

Toby Lowe: Yeah, thanks for that question. And I'm pulling up the guidance right now. We didn't include a firm definition. We included an example as you mentioned in one of the footnotes for molecular. And the intent was that that example would be applicable throughout. So while the exact example is talking about equipment that is used for molecular, the quantity if you will is generally applicable. So I think this is the footnote that says two 384 well thermocycler runs per eight hours. And so you would expect similar throughput for serology tests.

Gail Javitt: So about 100 per hour if we're trying to extrapolate?

Toby Lowe: You might have just done math faster than I did in my head. But yeah, if you're extrapolating that out to how your serology test runs, then yes. That would be how we'd suggest to consider that.

Gail Javitt: Great, thank you.

Toby Lowe: Yep.

Joseph Tartal: OK, let's go to our next question. Wenli, I'm opening up your mic. Please unmute yourself and ask your question.

Wenli: Thank you very much for taking my call. And I'm from XYZ Laboratory. And I have a general question on the reagent's stability. So according to the antigen template, it said the real-time reagent's stability study usually you don't need to be completed at the time of EUA issuance.

So then this also reagent's stability claims should not exist for four to six months. All right, so there's always accelerated study that can be done to claim for up to six months stability. My question is timing-wise, basically, when we submit the EUA, we don't need to present any stability test, a real-time stability or even accelerated stability test, or do we have to provide the accelerated stability test?

And then during the interactive review, usually, we don't have to present the stability test at that time. During the interactive review, do we have to perform the accelerated test to claim the four months or after six months? Or another scenario so we don't need to do any accelerated study. We will automatically claim four months stability. And there were, of course, immediately started the real-time stability study as soon as the US authorized. So this timing and what must be done in the question here?

Timothy Stenzel: Yeah, so we would consider an application as complete if it includes not just stability data, and it can be accelerated stability data, and obviously, with accelerated data at storage at a higher temperature, it doesn't take as long as real-time stability data. We would consider an application that

doesn't have some stability data and the stability testing protocol as being incomplete. And we would be unlikely to review that application until it has that.

So we would recommend that you include at least accelerated stability data in the application along with your protocol for both how you did the accelerated stability testing and your plan and real-time stability testing protocols so that we can review. We still are getting a lot of applications. And we are expecting complete applications in order to initiate the review at this time.

Wenli: OK, so basically, we still need to include some sort of reagent stability testing or either accelerated or some kind of real-time test in the submission, is that right?

Timothy Stenzel: We're not requiring real-time data in the submission. If you have it because you've launched your test outside the US and you have a longer dating than what can be supported only with accelerated stability then we want to see it. What we want to see is, at the very least, accelerated stability testing data justifying your first expiration dating time and your protocol for the accelerated stability testing and your planned study for real-time stability testing.

Wenli: Got it, thank you very much.

Timothy Stenzel: Mm-hmm.

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

Rachel Liang: Right, thank you for taking my question. My question is for point-of-care molecular test. Is it generally acceptable to use a computer assay that is authorized only for symptomatic testing for an Alzheimer's study so a clinical evaluation consisting of asymptomatic and symptomatic patient populations?

Timothy Stenzel: I'll turn this over to Toby and request for responding.

Toby Lowe: Hi, I believe this is another one that was sent in ahead of time by email. And we will send a response by email.

Rachel Liang: OK.

Toby Lowe: Since it was a very specific question with multiple parts to it, but we will get your response by email.

Joseph Tartal: OK, thank you. I'm going to go to our next question. Laura, I'm unmuting you. Please unmute yourself and ask your question.

Laura Poling: Hello, this is Laura. I have a molecular device for at-home use and possibly point-of-care, do I still have to have a PI oversee those studies even though home-use and point-of-care would not have such oversight?

Timothy Stenzel: So IRB authorization is the firm's responsibility. And we're not checking them for EUAs. But it is good to do to protect your firm and the test developers in case of any injuries. We know of

reports to poison control, for example, of kids ingesting some of the reagents in the kits. And so these kits in the home are not always totally benign. But we do not check IRB status for our reviews for EUAs.

We do have expectations for non-EUAs. It's a different question. But certainly, it would be my recommendation that you would have everything under IRB authorization.

Laura Poling: OK, thank you.

Joseph Tartal: OK, let's get to our next question. Jennifer, I'm unmuting you. Please unmute yourself and ask your question.

Jennifer Stanford: Thank you, sorry that I'm chiming in on this so late. This is my first Town Hall. So you may have answered this question before. But how are you handling children under the age of 18? Are you requiring an ascent, or if the IRB that we have used for our protocol is fine with the parent consenting for anyone under the age of 18, is that acceptable?

Timothy Stenzel: Under the age of 18 years, not 18 months or 18 years, right?

Jennifer Stanford: Right, 18 years, yes.

Timothy Stenzel: So again, having to do with IRB consent, we would defer to what the IRB thinks. And we are not checking IRB status or IRB consents for EUAs at least at this time. And so we would defer that question to the IRB that you're using.

Jennifer Stanford: OK, that's great. The IRB for this short, over-the-counter self-test did not feel like an assent was necessary as long as the parent was there and consenting for them. So that's what we are doing. So I want to make sure. Thank you.

Timothy Stenzel: All right, thanks.

Joseph Tartal: And we'll take one more question. Vitale, I'm unmuting you. Please unmute yourself and ask your question. And this will be the last question of the Town Hall.

Vitale, I see you're unmuted but I cannot hear.

Timothy Stenzel: No, I don't hear anything Joe.

Joseph Tartal: OK, sounds like then that is it for our live questions of today. So thank you, everyone. Thank you both for the participants and the attendees as well as for the great answers provided by our panelists. We greatly appreciate this discussion and all the participation.

Today's program and transcript 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 Town Hall and COVID-19 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. So please, complete a brief survey, which you may find at www.fda.gov/cdrhwebinar. Also, please remember to join us for the next IVD Town Hall scheduled for Wednesday, February 23, 2022. This concludes today's program, thank you.

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