

**Virtual Town Hall #72  
October 20, 2021**

**Moderator: Joseph Tartal**

**Joseph Tartal:** Hello, and thank you for joining us today. I'm 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 72 for SARS COVID test developers, in which we'll discuss and answer your questions about diagnostic tests and the fight against COVID.

The next IVD town hall will take place next month on Wednesday, November 17th. Today's presentation transcript will be made available at CDRH Learn under the subsection titled, Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. Please note that all the recordings and transcripts to date are now available. Our panelists for today's program are Toby Lowe, Associate Director for Regulatory Programs in the Office of In Vitro Diagnostics and Radiological Health or OIR, and CRH's Office of Product Evaluation and Quality, and Dr. Kristian Roth, also from OIR.

We'll begin with opening remarks from our speakers. And then we'll answer your previously emailed questions about COVID test development and validation. And then finally, we'll open the lines up to your live questions. To ask a live question, please select the Raise Hand icon at the bottom of your screen. Please wait until we get to that time to raise your hand. When you're called on, please identify yourself and ask your question promptly. Also please note we are not able to discuss any specific submissions that are under review. Now I'll hand the program over to Toby. Welcome, Toby.

**Toby Lowe:** Thanks, Joe. And thanks, everyone, for joining us again this week. We have just a little bit of in the way of updates. And then we'll do our prepared questions that we received ahead of time, and then jump into the live questions.

So I believe at the last Town Hall, we mentioned the letter to health care providers about the Abbott Alinity potential for false positive results. We have since issued, or classified rather, the Abbott recall for that issue. And also, we clarified in the letter to health care providers and the recall notice, that the recall is to update the software. The actual test kits do not need to be returned. And they can continue to be used with the updated software.

We also discussed last time, the updates that we made to our FAQ about priorities. I just want to reiterate that for anyone who may have missed it last time. We have updated our FAQ about priorities to be clear that we are prioritizing at home and home collection tests for diagnostic tests-- so molecular and antigen-- and not for serology tests.

So with that, we've also removed the corresponding template from our website so that there's no confusion there. And we are generally declining to review EUA requests for home collection and at-home serology tests for the time being. If that changes in the future, if we determine that there's a public health priority to review those, we will announce that accordingly.

So we also, last week, announced that we had updated all of the templates available on our website. So those are obviously still there. And we will continue to update those as we have new recommendations to share. And along the update with prioritizing at-home and home collection tests, we are, as we've

discussed in the past, we really are focusing on increasing availability for over-the-counter rapid at-home tests. And we will continue to update recommendations to help facilitate additional availability. So please keep an eye on the templates. Because that's where we'll be updating those recommendations.

And with that, I will move into the questions that we received by email. The first one is about an at-home antigen test, an over the counter antigen test, asking whether OTC assays could use an approach similar to some of the authorized tests with symptomatic only in the clinical validation study, with a condition of authorization to evaluate asymptomatic individuals and use that approach to be authorized with a serial screening claim.

And yes, that that approach is outlined in the Supplemental Template for Developers of Molecular and Antigen Diagnostic COVID-19 Tests for Screening with Serial Testing. It's a very long template name. And that does outline that approach. We do recommend that you at least attempt to include asymptomatic individuals in your clinical study. But if you are not able to get the recommended numbers, then we suggest you look at that template as an option. And we would include a post-authorization commitment or post-authorization condition to further evaluate with asymptomatic individuals.

The next question we have is regarding serology home collection. So as I just mentioned, we are not currently prioritizing review of EUA requests for serology home collection. So we generally would decline those EUA requests. And those should not be offered, since we do require authorization for any home collection test prior to being offered. They do not fall under the notification policy in the guidance.

Our next question is regarding a molecular at-home test and the analytical validation. Kris, do you want to take this one?

**Kristian Roth:** Sure. So this is about the analytical validation studies for SARS-CoV-2 assay that have been designed in compliance with the template, which was now of course, updated recently. So these new template sections are related to kind of the standard material that we're requesting folks to test. And the standard material testing section is kind of independent from the LOD.

So that LOD test material can be a variety of different compositions. And I think those compositions are noted in the template. And the additional testing of a standard material is going to be added to the condition of authorization. So that's of course, after you received the EUA. And then if you prefer to complete this type of work prior to authorization, there are potentially other routes available. And I think those are available to you. And I think we would consider that type of approach on a case-by-case basis. And if you just want to send that in with a particular standard material in mind, that's something that we can consider it as an alternative approach.

**Toby Lowe:** Great, thanks Kris. So the next question that we have is about again, language in the updated molecular template, regarding non-SARS-CoV-2 comparator assays. This is for multi-analyte tests, such as those that include influenza. The question notes that the number of available comparator assays is very limited and that some do not provide CT values. So they're asking whether there's any flexibility in the requirement, which states that the clinical performance for the non-SARS-CoV-2 analytes, such as influenza and RSV, should be determined by comparison to an FDA-cleared molecular test, specifically that we recommend using an FDA-cleared molecular test with prospective clinical study data from the past five years as the comparator.

So we do recommend that the comparator for flu be an FDA-cleared device. And the CT values are important to ensure that there's a range of low to high positives. So if the comparator method does not provide CT values, we would recommend that you discuss with us, alternate ways to establish low positives. Notably, that's a different approach than our typical approach for flu 510(k)s, since those 510(k)s typically include a prospective clinical evaluation, which ensures that the samples are representative of the patient population.

Without the prospective study design, we need something like the CT values to ensure that the samples are representative of the full range of patient populations. And we do recommend if you're having difficulty sourcing an appropriate comparator. That you reach out to us to discuss that, what you've done to try to get that comparator, and discuss an alternate proposal that you may have. Anything to add on that one, Kris?

**Kristian Roth:** No, I think you covered it. Thanks. It is a little bit of a moving target. And we understand that. And so we do want to be flexible in how those samples are characterized. So if you have another alternative proposal, we would be happy to hear it.

**Toby Lowe:** Great, thanks Kris. The next question is regarding the updated molecular template, stating that candidate tests should demonstrate a minimum of 95% positive and negative agreement for all sample types requested, and asking if a clinical study is conducted with NP swabs or samples, nasopharyngeal samples, will the intended use still be inclusive of mid-turbinate and anterior nasal swab samples? So for SARS-CoV-2 tests as long as you validate to 95% for the most challenging matrix in the category, so upper respiratory or lower respiratory, all common sample types in that category are generally included in the authorization. However, for multianalyte tests, we have seen data that there may be differences between specimen types especially for mid-turbinate. So we would want to see mid-turbinate swabs separately validated if requested as a specimen type. Nasopharyngeal validation may still support an anterior nasal swab claim for multianalyte test that includes influenza but we would want to see those mid-turbinate swabs validated separately. Anything to add on that one, Kris?

**Kristian Roth:** No, thanks.

**Toby Lowe:** All right, so continuing the theme of multianalyte tests, the next one here is asking about the ability to acquire contemporary flu positive specimens given the low prevalence of influenza from 2020 to date and related challenges associated with that low prevalence. So asking whether FDA would consider the use of contrived samples for flu A and flu B to enrich a prospective clinical sample-- to enrich the prospective clinical samples that they are able to collect to support an EUA for molecular SARS-CoV-2 plus flu A and B multiplex tests. Or if FDA has other recommendations for population enrichment strategies given the low prevalence of influenza.

So we do recommend for the evaluation of clinical performance of your COVID-19 and flu combo test that a prospective clinical study should be conducted for at least two weeks. After that two week duration, a clinical validation study using banked samples could be conducted at one of your testing sites. We would recommend that you use archived positive and negative clinical samples. And we do acknowledge that the reduced prevalence of influenza last season makes archived specimens difficult to obtain but we are still recommending using those archived samples to support authorization.

Evaluations with contrived samples are not adequate to support clinical performance of those diagnostic tests at this time. And we would also likely include a commitment to complete a post authorization clinical study depending on what you are able to collect and validate prior to authorization and that would be discussed during the review of your EUA. Anything additional there, Kris?

**Kristian Roth:** I just want to comment on that post authorization commitment. I think if you look at some of the previous letters of authorization for tests such as these, you'll notice that there is language in that commitment to adjust the time frame as needed. So certainly over the summertime, flu is very rare. Let's hope it stays rare now here through flu season. So I think there are opportunities to adjust the time frame to match the observed prevalence of flu in the US currently. Thanks.

**Toby Lowe:** Thanks, Kris. Our next question is asking about FDA guidance on certain definitions-- symptomatic and asymptomatic COVID-19 subjects, COVID-19 positive cases, and high-risk individuals. So for those definitions we recommend that you refer to the CDC's website where they do have those definitions listed.

And then this question also asks about FDA's expectations to grant marketing authorization for a COVID-19 rapid diagnostic test in terms of the studies to perform in comparison to studies required for an EUA. We have not yet granted full marketing authorization for a rapid antigen diagnostic test so we do generally recommend that you submit a pre-submission to discuss your approach for a De Novo request.

We have, as we've talked about previously, granted full marketing authorization for a molecular diagnostic test and that decision summary is available on our website and is very helpful for developers to take a look to see the additional information that we're looking for, for a De Novo in comparison to an EUA there.

And then our last question here for today is about a point of care molecular diagnostic test related to the preparation of their clinical study for prospectively collected anterior nares swab samples. And the template mentions the participation of four to six test operators. And the question is asking for clarification on the distribution of test operators across two different test sites. So generally we do, as noted, recommend that at least four to six operators that are representative of the intended use are included for point of care tests. And generally we would expect it to be best if possible to include multiple operators at each site. So two and two, two and three, three and three. And if you have an alternate proposal for that we would recommend that you reach out to us to discuss.

So with that, I think we can kick it over to live questions.

**Joseph Tartal:** Thank you, Toby. So we'll go to our live portion of the program. So please if you have a question, raise your hand. I will take the questions in order of those hands raised. So the first question is from Shannon Clark. I'm going to unmute you in a second. Here we go. You've been unmuted. So please unmute yourself and ask--

**Shannon Clark:** Hello. Can you hear me?

**Joseph Tartal:** Yes we can.

**Shannon Clark:** Hi, it's Shannon Clark with UserWise Risk Specialists in Human Factors, and my question is about point of care testing for a home-- for point of care use of an antigen rapid test kit. The new template notes that we're able to use retrospective sampling specimens and I was just wondering if there's an expectation that we expose various health care providers to the same prevalence of positives as you would see in the community or in perhaps a worst case county in the United States, or whether we can simply randomize exposure to the positive versus negative specimens which would shorten the study a ton compared to just reflecting the general population. Does that make sense?

**Toby Lowe:** So I'm not sure that I fully followed your question there, so let me see if Kris did, and then if he did he can take it and if not I'll ask you to rephrase a little bit.

**Kristian Roth:** I think so, yeah. I mean it is a fair point. I think in the ideal-- OK, let me just back up for one second. I think the most important piece is that it is performed in a PoC setting in a manner that is kind of in addition to the workflow that that study site is performing already, right. And so I think that's the spirit of this, the PoC evaluations to ensure that-- these folks are busy. They've got multiple priorities and now this is yet another thing that they're being asked to do. So the study should reflect that type of use case.

So what you're saying is does it have to the positivity rate need to reflect what it is in the United States right now or locally. And I think there would be some flexibility there. Certainly a 100% positivity rate is likely not acceptable. Even 50% is probably too high, so I think we'd be willing to entertain a higher positivity-- quote unquote positivity rate in that study to facilitate a quicker evaluation. What that number is I think that would be something we have to discuss within the context of the study.

**Shannon Clark:** OK. And in your ideal state would you expect that use of these test kits is observed by perhaps human factors, moderator or observer. Or is now the expectation that these individuals would independently just use the test kits. I mean, I guess my concern is that you want them to be untrained and if we just unleash them into their context of use they're likely to discuss amongst themselves and train each other. Does that bother you at all?

**Kristian Roth:** That's an interesting point. You know human factors is important and ensuring that you're getting information from the study to ensure that that test is being run appropriately is important. Also, there may be changes that could help improve test performance. So I don't believe it's a requirement for observation but certainly it sounds like a good practice. We haven't really discussed the inner workings of the laboratory and folks kind of training each other. It is an interesting point but it's something we really have not considered as far as--

**Shannon Clark:** Yeah, it's really a trade off. Either you can do real life use or you can control for these variables that you're looking for. I don't see any opportunity to do them both.

**Toby Lowe:** Yeah and I think-- thank you-- also important to consider that that is real life usage and that would be representative of what might happen in a real use setting.

**Shannon Clark:** For them to train each other, OK. Thank you.

**Toby Lowe:** Sure.

**Joseph Tartal:** Thank you for your question. We'll take our next question. Tianyang Liu, I'm going to open up your mic. Please unmute yourself and ask your question.

**Tianyang Liu:** Thank you. And my question is that of course, the FDA EUA template for OTC product require that all of the patients, I mean participants, need to take the SOC first. And do FDA-- do the agency right now have specific requirements for what type of SOC should the participants take? I mean--

**Toby Lowe:** So, I think what you're referring to there is the recommendation for ordering-- for ensuring that there's specified order for which sample is being taken first and that standard of care would always be taken first. We do recommend that the standard of care sample always be taken first just to ensure that there's adequate patient care. But that is I believe, generally referring to the situations where the comparator test is being used as the standard of care. So we don't specify what the standard of care should be. We're referring to when the standard of care is-- when the competitor rather is being used as the standard of care we wouldn't want you to randomize the order of collection. Kris, anything to add on that?

**Kristian Roth:** Yeah, I think in some cases, if the user is collecting their own sample there should be considerations that user isn't being trained kind of on the spot to collect their samples. So if you have the opportunity to have that self-collection happen immediately after the standard of care that's probably a least biased sample collection procedure. Certainly, some folks have randomized and that's acceptable as well, but I think I would say keep in mind the kind of self training aspect of that swabbing.

**Tianyang Liu:** Oh so what do you mean-- to see if I understand you right. So what do you mean that the SOC standard of care may give a bit of training for the self-use patient. And in fact this small bias is acceptable by the agency right now. Is that--

**Kristian Roth:** So nothing should get in the way of patient care, right. So if the physician needs to take a sample to manage that patient, that should be of course the first priority and it should be done without delay.

Then, if there's a study going on and you have the appropriate patient protections in place, then you could start talking about what else are we doing to this particular patient?

**Tianyang Liu:** OK, OK. Got it. Thank you very much. And actually, I have another question I'm not sure if that I could ask it right now or I should wait in the line and wait for my turn again.

**Joseph Tartal:** It looks like we have plenty of time to come back around. So if you don't mind, we'll go to the next question and then just raise your hand again.

**Tianyang Liu:** Sure.

**Joseph Tartal:** Thank you. So our next question is from Joshua Levin. Unmuting you right now. Please ask your question. Please unmute yourself and ask your question.

**Joshua Levin:** Hi Kris and Toby, this is Josh Levin from Cell. I wanted to follow up on a question that was asked, one of the email questions, and I wanted to make sure that I heard correctly. So asymptomatics, either positive or negative asymptomatics, are not required prior to authorization for an OTC home use test. Is this correct?

**Toby Lowe:** So we do recommend in the template that your clinical evaluation include all comers, asymptomatic and symptomatic, when you're seeking an over-the-counter test. If you are not able to get asymptomatic individuals in your clinical study then the supplemental template for serial testing does include an option for serial testing authorization with only symptomatic individuals having been evaluated, and then a post authorization condition to evaluate in asymptomatic individuals.

**Joshua Levin:** OK, so if we wanted to follow the supplemental template it would be acceptable to do a study with just symptomatic patients with that serial screening claim?

**Toby Lowe:** Yes, that's right. We would recommend that you try to get a broader population, but that is an approach that we have included as an option.

**Joshua Levin:** OK, thanks for the clarification.

**Toby Lowe:** Sure.

**Joseph Tartal:** Thank you. Our next question is from Gordon Siek. I'm unmuting you now. Please open up your mic and ask your question.

**Gordon Siek:** Hi, can you hear me, all?

**Joseph Tartal:** Yes, we can hear you.

**Gordon Siek:** OK, my question is specifically about the antigen test. And you mentioned that for the non-LOD studies for example that-- I'm assuming the endogenous interference studies for example-- that you would be open to alternative standard materials not inactivated virus like I guess recombinant or purified N-protein-- we're doing an N-protein assay.

**Kristian Roth:** So I think your best bet here is to follow the template and whatever materials are listed in that template is acceptable-- are certainly acceptable. If you have alternative approaches, that's something that we likely would want to follow up with an email or pre-EUA and make sure that we completely understand the material that you're proposing and the use for it just to make sure that all the details are kind of captured. Yeah, that's what I would recommend. So--  
[INTERPOSING VOICES]

Sorry, go ahead.

**Toby Lowe:** No, go ahead.

**Kristian Roth:** Well, use the template inbox. Again, you can highlight this as something that came in from the town hall and we can give you written feedback fairly quickly. Thanks, Toby.

**Toby Lowe:** Yeah and just to further clarify, the discussion that we had earlier about the standard material testing was referring to some information in the molecular template not the antigen template. So you do want to make sure that you're taking a look at the antigen template if that's the type of test that you're developing. And the discussion about alternate materials related to the standard material testing for molecular was referring to what we generally include as a post authorization condition to

evaluate the analytical limit of detection and traceability with an FDA recommended reference material. So that is different than the pre-authorization validation that we would expect.

**Gordon Siek:** OK, thanks for clarifying that. We are planning to use virus.

**Joseph Tartal:** OK. Thank you for the question and we'll move on to our next question. Homer Wu, I'm going to unmute your microphone right now. Please unmute yourself and ask your question.

**Homer Wu:** OK, you guys can hear?

**Joseph Tartal:** Yes, we can hear.

**Homer Wu:** OK, thanks for taking my call. My quick question is, according to the templates if we apply for serial testing for home use antigen we have to supplement the pre-EUA. Is that right or we can go ahead without the pre-EUA?

**Toby Lowe:** So if you're following the template then you could do that without a pre-EUA. You can just submit your EUA request. There is discussion of serial testing in the supplemental template as well as in the antigen template directly or the home use template rather. If there are questions that you have or approaches that you want to take that are different than what is in the template then we would suggest that you come in and discuss that with us.

**Homer Wu:** OK, so it's not required, right?

**Toby Lowe:** A pre-EUA is never required. It's just an option if there are questions that you need to get answered prior to submission of your EUA request.

**Homer Wu:** OK, follow up question. If we do apply for the pre-EUA, what's the time frame not to have a response?

**Toby Lowe:** We are not able to provide a time frame at this point. We do have some information on our FAQs about our prioritization and about the time for reviews but we're not able to provide an estimate right now.

**Homer Wu:** OK. All right, thank you guys.

**Toby Lowe:** Sure.

**Joseph Tartal:** OK, next question. Laura Ferguson. I'm muting you right now. Please unmute yourself and ask your question.

**Laura Ferguson:** Thank you for taking my question. It's with regard to the new updated template for molecular testing. And it's Section J6 which is the expansion of the sample stability study requirement. I'm wondering what prompted the FDA to add this additional requirement of a study, specifically studying the stability of the samples prior to testing. And if we are designing a study to meet this new requirement if samples that are freshly arrived in the lab are considered fresh and those that are not stored overnight at 4 degrees say are considered those that have been stored as opposed-- that that



would be the two conditions for our study of freshly arrived in the lab and second to that being stored overnight in the lab in the refrigerator. Thank you.

**Toby Lowe:** Thanks for that question. Kris, is this something that you can take?

**Kristian Roth:** Sure. You know I think sample stability should reflect-- the time frame of that should reflect the actual time frame that the sample has been exposed to. So if it has been in the refrigerator for overnight then that's no longer t-zero. You can contrive samples for sample stability and that will give you a little bit more predictability about time zero and the value or the-- sorry-- the quantity of virus at time zero. So that may be an option. That could be an option for you.

**Laura Ferguson:** And what was the reason for adding this requirement to the study-- to the template?

**Kristian Roth:** For adding sample stability?

**Laura Ferguson:** Yes, the specific requirement for doing a separate study as opposed to simply referring to the CDC document.

**Kristian Roth:** Yeah. Honestly we've seen issues of sample stability. Any time you take that sample the clock is somewhat ticking as far as how long that virus is going to be stable, the RNA is going to be stable, protein going to be stable. So really this is a standard evaluation we do in the 510k world, PMA world. And I think we were getting enough information from the field that stability was something that could be different. So we also have new samples. We have saliva samples now for SARS-CoV-2. We never really had saliva for upper respiratory samples. Certainly folks are transitioning from VTM to saline or PBS, so that was something we want to make sure we understood a little bit better. So it's really driven by a multitude of factors.

**Laura Ferguson:** OK, thank you.

**Joseph Tartal:** OK. We'll move on to our next question. erozen, I'm opening up your mic. Please unmute yourself and ask your question.

**erozen:** Hello. Good afternoon. This is Elliot Rosen on behalf of [INAUDIBLE] and MiCo Biomed. A quick question regarding the guidelines for test developers, serology tests, for neutralizing antibodies. The guidelines were recently updated. We were working on a clinical trial and we were working off the initial March guidelines, and as a general question we were wondering if there's any contradiction between the two guidelines, if we need to update our protocol to comply with them. And specifically, the new guidelines mention that manufacturing QSR requirements may not be waived, and just wanted to know if that's something we should follow for the updated guidelines rather than for the initial guidelines that were again released back in March.

**Toby Lowe:** Thanks for that. So yeah, I mean if you've done all of your testing and validation under the old template and something has changed, that's probably something that we can discuss with you during your review to see if there's anything that needs to be updated. And specifically regarding the QS requirements, that is again something that could be addressed through the review.

**erozen:** And just as a quick follow up question. And you might not be able to answer this, but would your recommendation then to be to not change anything at the present time and wait until the submission is actually completed or--

**Toby Lowe:** Yeah I think if there are things that are-- without knowing exactly what aspects may be applicable here-- if there are sort of smaller updates that are easy to incorporate maybe to language and things like that, please go ahead and include those in your submission. If it's a matter of redoing validation completely, please submit your EUA request as you've prepared it so far and then we will discuss with you during the review.

**erozen:** Understood. Thank you very much.

**Toby Lowe:** Sure.

**Joseph Tartal:** Thank you, Elliot. Our next question is from Eric Penney. Eric I'm unmuting your mic. Please unmute yourself and ask your question.

**Eric Penney:** Thank you very much. I have a really broad question about comparative testing. We're constantly told to pick from the top of the FDA's reference panel list, but that list has grown tremendously over the months. So for example, if I pick number 60 on that list, that's about exactly halfway through, is that still an acceptable assay or should I be picking from, let's say, the top 10 or 25?

**Toby Lowe:** Yeah, so we're not able to really sort of draw a line there. It really depends on the circumstances of what's available at what time and what's changing with the pandemic as things progress. If you're looking at something that generally has higher sensitivity, it's likely to be acceptable. If you have a specific test that you're considering and you want to confirm that it would be acceptable you can always send that into the EUA templates mailbox and we will take a look at that for you.

**Eric Penney:** And I know you can't really state a cutoff, but is there a preferable LOD range out of that group?

**Toby Lowe:** Yeah we're not we're not really able to provide that at this time.

**Eric Penney:** Of course. All right, thank you so much.

**Joseph Tartal:** OK, thank you. Our next question from Yu Zhao. I'm opening up your mic. Please unmute yourself and ask your question.

**Yu Zhao:** All right, thank you so much. I have two quick questions related to our home use rapid test kit with mobile app. The first one is related to FDA template for the antigen test for non-laboratory use. There's a requirement for test results reporting and it says our test results will be reported to health care provider and public health authorities using appropriate LOINC and SNOMED. Is this required for at-home use kit?

**Toby Lowe:** So the reporting discussion in the template is, it's important because reporting to public health authorities is important for tracking the cases across the country. But there is only a requirement-- there's reporting legal requirements that do not fall under FDA so I won't get into that in specific detail, but those requirements are generally for laboratories and practitioners. Their requirements are not the

same for a home user but we still do want to encourage reporting. And so the recommendations in the template are to encourage incorporation of an easy reporting option. And that is something that we have and will continue to include as a post authorization condition in certain cases where reporting is not able to be incorporated pre-authorization.

**Yu Zhao:** OK, thank you for clarifying. My second question is more generic one. My client is a European company and they did a clinical evaluation usability in English-speaking participants back there. In general, is that acceptable if such studies were conducted in a way that's very close to FDA recommended? Is this acceptable not to repeat clinical evaluation usability in the US for EUA purpose?

**Toby Lowe:** And you said that was for a home test?

**Yu Zhao:** Yeah, for home test.

**Toby Lowe:** Yeah, so we do generally want to see those studies done in the US. We are working on ways to make that more accessible for developers especially for developers that are outside the US. But we also would encourage you to come talk to us if you have an alternate proposal or if you're struggling to get that done so that we can work with you on that

**Yu Zhao:** OK, thank you so much.

**Joseph Tartal:** Our next question is from Tianyang Liu. Tianyang Liu, I'm unmuting you. Please ask your question.

**Tianyang Liu:** OK, thank you. So my second question is actually I'm wondering that if there is other ways than email for interactive communication for an EUA application this time if the email communications is not fast enough.

**Toby Lowe:** So once you're under an interactive review with a lead reviewer assigned to your submission, you can work with them directly. If there are times when you would prefer to have a phone call you can ask for that and they may or may not be able to accommodate that depending on their workload and their schedule, but we definitely are interested in making sure that there is clear communication. So we can work with you on that depending on the situation.

**Tianyang Liu:** OK, great so that actually we could email our reviewers to require a Zoom call or other ways, phone call or something to accelerate the process, right?

**Toby Lowe:** So you can request that and we'll do our best to accommodate it as schedules permit.

**Tianyang Liu:** OK, thank you very much.

**Joseph Tartal:** Our next question is from Shannon Clark. Please unmute your mic and ask your question.

**Shannon Clark:** Hi, Shannon Clark with UserWise. My question-- so we're experts in human factors and generally when you have a time frame and instructions for use, it's to be assumed that users are not going to meet that time frame. For example, holding down an auto injector for 15 seconds, we all know that they're not actually going to hold it down for 15 seconds. Likewise, if we instruct them to swab for 15 seconds, they're not going to hit 15 seconds I heard that the CDC, FDA-- not sure what entity is

running a study to look at variability in swabbing as it affects outcomes-- is this study in fact happening and would it evaluate that parameter of duration swabbing? And if so, can we leverage that in some way? And then finally, what do we do with data in which users are not swabbing for a full 15 seconds for OTC clinical testing in human factors?

**Toby Lowe:** Yeah, so we do have recommendations for flex studies in the templates. And the flex studies are intended to get at just that. If there's a recommendation for 15 seconds we want to see sort of the range that will still give you an appropriate response. There are various efforts throughout the US government to do some additional studies. I'm not sure that there's much I can say about what studies may or may not be ongoing. I don't know of all of them. Different people are involved in different things but that's something where if that type of information is evaluated and becomes available we would make sure that that's communicated.

**Shannon Clark:** But isn't the data in your clinical study the closest you'll come to a flex study in relation to this question because there was going to be variability in user behaviors? Or do we need to run an additional clinical study where we recruit a variety of users with a variety of ethnicities, et cetera to answer this question?

**Toby Lowe:** So if you take a look at the flex study recommendations in the template, those can be done in the laboratory. Those don't need to be done with lay users. So you can look at-- and I'm not sure if swabbing is actually included in the flex study design recommendations, but that is certainly something that you could consider doing there. But the way that flex studies work generally are that you would have a laboratory and look at it and sort of test the range of times that that might be expected to see when performance drops off.

**Kristian Roth:** And I could just add one comment there. These flex studies are performed in a controlled manner and so the outcomes and the observations are kind of testing a hypothesis whereas if you're doing clinical study, yes, of course, there's going to be variability in how that test is being used. But it's difficult to draw any conclusions about what was actually kind of studied. So that's why the flex thing is much more appropriate to kind of look at the edge cases as far as use is concerned. Thanks.

**Joseph Tartal:** Thank you, Kris. And thank you, Shannon for your question. Due to time we only have about five minutes left and about four questions so we're going to move on to our next participant. Rosemary, I'm muting your mic. Please ask your question.

**Rosemary:** Yes, hi. Hi, can you hear me?

**Joseph Tartal:** Yes.

**Rosemary:** Yeah, thank you for taking my call. I just have three quick questions on wet testing for cross-reactivity under molecular diagnostics. The first thing is, is there a requirement or recommendation on the re-suspension matrix for this cross organisms, VTM, PBS, or even tris buffer. The second is, is there a recommendation for the number of replicates for each test organism? And the third is, is there a requirement or a recommendation for the number of strains per organism for testing?

**Toby Lowe:** Thanks for that. There are recommendations in the template regarding this testing. And since your questions are fairly detailed, I would suggest you take a look at the recommendations in the

template. And if your questions are not answered there you can send that into the templates email so that we can provide additional clarity.

**Joseph Tartal:** OK, thank you. Our next question is from Vitali Karaliou. I'm opening up your mic. Please ask for a question.

**Vitali Karaliou:** Thank you so much. Another broad question. Would EUA be still a viable pathway for new molecular in lab tests with certain technical economic advantages, let's say high throughput simplified fast analysis protocol or should we consider the 510K pathway considering by as far as De Novo. They have rather unique testing approach. So just want to ask you this.

**Toby Lowe:** Yeah we have continued to prioritize in lab molecular tests that have the ability to increase testing capacity. So as you mentioned high throughput, and if you have questions of whether your test would be prioritized you can send some of the details in to the template mailbox and if there's enough details for us to make that determination we can let you know.

**Vitali Karaliou:** Thank you.

**Joseph Tartal:** OK, our next question is from J. Mullally. I'm opening up your mic. Please unmute yourself and ask your question.

**James Mullaly:** Hi Toby and Chris, this is former FDAer Jim Mullally, now at MCRA, that's M-C-R-A. Nice to hear your voices again. I have a follow up question to your comment about OTC antigen studies being an all comers study. So there are several EUAs that are authorized that clearly state in the labeling that their respective studies had recruited symptomatic subjects and they don't have any asymptomatic study subjects in their study. So I just wanted to clarify whether this study design, one in which recruiting only symptomatic subjects, would be acceptable acknowledging that there would be a condition for authorization to support asymptomatic claims?

**Toby Lowe:** Thanks, Jim. Good to hear your voice as well. Yeah as we mentioned earlier, the preference is to try to recruit both symptomatic and asymptomatic. But as is discussed in the templates, if you are only able to get symptomatic there is the option for serial testing so that we can-- and then we would include, as you mentioned, the post authorization condition.

**James Mullaly:** Great, thank you so much.

**Toby Lowe:** Sure.

**Joseph Tartal:** OK. And our last question of the day from Richard Montagna. I'm going to open up your mic. Please unmute yourself and ask the last question.

**Richard Montagna:** OK, thank you. I have previously called in about some efforts that we are doing right now to shorten the assay. It's a currently authorized PCR assay. And most of those changes are software. There may be some buffer changes. And when I originally called in which was several months ago, Tim Stenzel had indicated it would be acceptable if we compared the current assay that we are currently authorized with the revised assay using the same sort of parameters we use when we were first authorized, which was back in April of 2020. Now with the new templates out there, it looks like there's additional aspects that one would look for. How would we be treated? Would it be acceptable to just--

like we had contrived samples in the past. We ran the various interference studies, et cetera, or would we have to look at more expansive studies under the new template?

**Toby Lowe:** Yeah, I think that's something that we would suggest you reach out through the templates mailbox since it is very specific to your case. But generally we would expect your comparator to meet the comparator recommendations in the template. So without knowing the specifics of your test data however they do that we would generally expect that.

**Richard Montagna:** OK, thanks Toby. We'll do that.

**Joseph Tartal:** OK, and with that, that is the end of our program. Thank you everyone. We greatly appreciate your participation. Today's presentation and transcript will be made available at CDRH Learn. Please visit CDRH Learn at [www.fda.gov/training/cdrhlearn](http://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. Again, as previously noted, all of the recordings and transcripts except for today's are now available and we will work on making today's recording and transcript ready in the next few weeks. For additional questions about today's presentation and topics, please send an email to [CDRH-EUA-templates@fda.hhs.gov](mailto:CDRH-EUA-templates@fda.hhs.gov). As we continue to hold these virtual town halls we appreciate your feedback about the program series.

Please complete a brief survey which you will find at [www.fda.gov/cdrhwebinar](http://www.fda.gov/cdrhwebinar). Last, as a reminder, please join us for the next IVD town hall webinar that is scheduled for Wednesday, November 17th. And this concludes today's town hall.

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