

**Virtual Town Hall #70  
September 22, 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 70 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in the fight against COVID. The next IVD Town Hall will take place on Wednesday, October 6.

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, and Toby Lowe, also from OIR.

We will 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 line to your live questions.

To ask a live question, please select the Raise Your Hand icon at the bottom of your screen when it is time. When you're called on, please identify yourself and ask your question promptly. Also, please note, we are not able to discuss specific submissions that are under review. Now, I'll hand the program over to Tim.

**Tim Stenzel:** Thank you, and welcome all to this virtual town hall. We endeavor to help developers get EUA authorization as quickly as possible. That's what we do pretty much 24/7 these days and have done since January 2020.

A couple of quick updates, and then go into the pre-submitted questions. The first update is: those who are customers of Abbot Molecular Alinity tests for SARS-CoV-2, there is a SARS only in a panel. You would have received a letter from the company talking about a false positive issue. Also, the FDA did make a communication about this.

So there was a design issue with the Abbot Alinity m that resulted in confirmed false positive. Don't know the exact rate. So we do recommend that the prior two weeks of cases, that you look and see if you were to retest those positives to confirm the positive with another SARS-CoV-2 molecular test. The company thinks they understand the cause. The company thinks they have a fix. The FDA is currently reviewing that fix to see if it indeed works. In the meantime, the firm can launch that update into high complexity labs only, if those labs wish to have that update, while the FDA reviews the update and prior to EUA authorization. When the FDA updates the EUA authorization with a fix or a mitigation that can be extended to all labs, including moderate and complex labs, then we will do so, and the firm can go ahead and update the software in all those labs too.

The second update has to do with EUA submissions for antigen tests. As we stated, it's a high priority for us to review these submissions, particularly point-of-care and home tests. We have added more personnel from other EUA review areas onto the antigen team. And we are making a concerted effort to reduce the turnaround time for those submissions.

Some developers have started getting feedback. And we plan to get through all the current submissions as rapidly as possible. And we hope this becomes evident over the days and weeks ahead.

With that, I'm going to move into the pre-submitted questions.

The first question has to do with a novel amplified signal lateral flow device intended for home use. This device would be packaged with the test, extraction buffer, and a swab for self-collection. The question has to do with regarding the self-collection swab. And they're asking, do they need to use FDA EUA swabs, which were authorized by the FDA for home use for self-collection, or can they use any FDA-cleared swab and validate them for use with their device, both as part of the human usability and the clinical study.

So the FDA does recommend nasal swabs for home use. Mid-turbinate swabs may be used if safe, especially for children. Typically, for children, in particular there'll be some method to prevent the swab from going up too far.

NP and OP swabs are not recommended. Now, one second. So, bottom line is that swabs can be used that are FDA 510(k) cleared, as long as they're validated and part of the clinical and usability studies. So I think that addresses that question.

Next question is, in the FDA guidance document regarding pooling for molecular devices, along with supplemental templates for developers of molecular and antigen diagnostic tests for screening with serial testing, is it possible to get further clarification on what the Agency defines as consecutively-collected samples? For example, for the asymptomatic claim, less than 20 consecutively-collected asymptomatic positives and less than 100 consecutively-collected on negative samples. I think it was probably less than or equal to 20, less than or equal to 100.

One hundred negatives should be easy to get. Twenty, we will accept 10 pre-authorization with an agreement to collect 10 more at least asymptomatic positives after authorization. And then the question is, typically, does it mean that the same person subject to return to the collection site for consecutive collection of a new swab, multiple site visits. Does it mean to only test the initial sample in a consecutive manner?

Thank you for the clarification.

So, consecutively collected samples are all the samples that are collected from eligible and unique study subjects between the start and end date of the study. During the study, no samples from eligible subjects should be omitted from the analysis.

So, in other words, pick a time period from if you're using any method of having those samples. We don't want to have subjects drop out, unless there's an explanation and a reasonable explanation for it. If you were designing a serial testing validation study, we recommend reaching out through a pre-EUA, or to your lead reviewer, to discuss details. This kind of serial testing validation study is rather complex and should only be implemented with input from the FDA to avoid unnecessary burden.

Moving on to the next question. So this developer has previously submitted a Pre-Sub for a combined molecular SARS and flu device. The FDA advised to perform a prospective collection testing study for at

least two weeks. And if we were unable to obtain the required number of positives, particularly flu samples, we were advised to use bank samples.

And I would just add to this that-- and it should be easy to get all the negative samples that are recommended, of course. Going on with the question. Given that flu is nearly nonexistent-- this is true-- it may not be very prevalent at all in the world this next respiratory season-- and that will probably be good, but not good for developers to get samples. So we would like to ask the FDA after the two-week prospective time period of collecting and testing, assuming we got zero flu samples, is it possible then to supplement with all bank specimens, with the understanding that we do a post-market study with fresh samples when flu samples are more readily available?

Again, this is specifically for a molecular device. So to evaluate the clinical performance of your combined device, a prospective clinical study should be conducted for at least two weeks, as the questioner stated. After the two week duration, clinical validation study using bank samples may be conducted at one testing site. You should test archived samples, both positive and negative. We acknowledge the reduced prevalence of influenza last season and so far this year, and that archived specimens may be difficult to obtain.

However, we still recommend testing archived samples to support authorization. There will likely be a commitment for a complete post-authorization study, as discussed using fresh samples.

The antigen test validation in this situation for combined SARS and flu devices has particular challenges with it. And the FDA does recommend that you discuss your study design for that with the FDA first. There are challenges in using bank samples.

Moving on to the next question, this questioner says, we are working on a rapid test that aims to evaluate both total and neutralizing antibodies simultaneously. On one side of the test, we observe the detection of total antibodies. And the other side, we observe detection of neutralizing antibody. So some requirements for the, I would say, recommendations for the EUA for each test limits, the assessment of clinical performance agreement to the test simultaneously, for example, the total antibody template asked for 75 RT-PCR negative samples, while the neutralizing antibody test states that all samples should come from RT-PCR positive individuals, among other examples similar to that. In the case of trying to detect both total and neutralizing antibodies on the same test, as mentioned in the beginning, which EUA template does FDA recommend us using in this case? Is there any other recommendation that FDA would give us?

So I mean, this is a good question. And the requirements of validation for both the recommendations that we make are different for both. So the FDA does recommend that developers complete all portions of a template that are relevant to their test. So for the total antibody, follow the templates for recommendations for total antibody. For neutralizing, follow the neutralizing antibody template.

If there are validation recommends that are not covered in a single template but apply to your test, we recommend you provide the applicable sections from each template in a single EUA request. Since the validation and considerations for neutralizing antibody tests are different from binding antibody tests, the same samples may not be able to support all proposed claims simultaneously, and additional samples may be appropriate to validate multiple indications. For more discussion on study design aspects unique to this device, we recommend sending additional questions in through a pre-EUA.

OK, moving to the next question. During the last diagnostics town hall, there was discussion about amendments to EUA applications. I believe that it was stated that changes to an EUA-authorized test that are submitted to FDA as an amendment can be enacted at high complexity labs while the amendment is still under review with the FDA. For this week's town hall, could you confirm that this understanding of the process is correct and provide any additional details with respect to this policy?

So this question does reflect our policy. And I did mention this policy relative to the infield correction that Abbott Molecular is making for their Alinity m system for the SARS-only test and their SARS panel test. So as discussed in the previous town hall meeting, the COVID test policy guidance, as well as the FAQs on our website state, that unless and until an EUA is issued that authorize additional testing environments for a specific test under CLIA, use of that test is limited to laboratories certified to perform high complexity testing, including testing at the point of care when the site is covered by the laboratory's CLIA certificate for high complexity testing.

This applies both to new tests and unauthorized modifications. So, yes, while the modification policy for commercial manufacturers of diagnostic tests provides for developers to implement modifications where they're still under FDA review, the implementation is limited to high complexity CLIA-certified laboratories.

And that ends the last question and the FDA response. So we can move into the live question phase.

**Joseph Tartal:** Thank you, Tim. And we have our first hand raised from Rachel Liang. I'm going to now click on for allowing her to talk. Please unmute yourself and ask your question. So you now can unmute yourself.

**Rachel Liang:** Great, thank you so much. Hi, Tim. And thank you, Toby.

So my question is, our team is working on a point point-of-care molecular diagnostic test. And we're still in the process of running clinical trials. If we want to implement changes to our devices and test kits, do we need to complete our current original study design, as in prospectively collect those 30 positives and 30 negatives before we start a new trial with the updated device designs? Or can we terminate our study prematurely and start a new study design with the new device design?

**Tim Stenzel:** So let me just ask a clarifying question. So have you already launched and labs are using your first design?

**Rachel Liang:** Yes.

**Tim Stenzel:** So any commitments made for that device are important to complete. And that's because patients have been tested with that device. And the condition of authorization for that was prescribed.

And if there were to be any issues with the device, as it was for your first EUA submission, we would want to know that. So that's a commitment that your firm made at the time of authorization. And we do expect you to complete that commitment.

You may be able, through an innovative study design, test both devices at the same time. But not to have any bias, I suggest you run that study, the combined study design, through our FDA review staff,

your reviewer, perhaps, that was used for the initial device, to get their input before starting, just to make sure you're doing this in an unbiased manner.

**Rachel Liang:** Got it. And just so I understand correctly, we would need to finish our current study design, collect those three positives and negatives, and then in parallel we can also start with our new changes and designs for the devices and test kits in parallel?

**Tim Stenzel:** Oh, yeah, you can do those in parallel. And you could even-- I don't know how complex your study design is—even consider and testing with both devices, if your subjects are willing to do that and your clinical site staff are willing to do that.

**Rachel Liang:** Got it. And just one quick follow-up-- so would it be possible for us to start this new study design at the same study site? Or do we have to look for a new study site to conduct this repeat validation study?

**Tim Stenzel:** The same sites could be used, and they could be used. You could begin the new study after you finish the first, but maybe a little bit cleaner, easier for the study site to understand and not get confused. But again, if you were to want to do this, finish the commitment for the original device and start validation for the same device at the same time, maybe even on the same patients. There's no prohibition against doing that. We would just want to make sure that you're doing in a manner that is unbiased towards the new devices.

And obviously, you might get three swabs. I don't know the details of your procedure, whether it's a direct swab or goes into some sort of buffer and if the buffer is the same between the two devices. If you use a buffer first and the buffer is the same between the two devices, then you want the tests done in a manner in which the person performing the test doesn't know the result for the other sample.

So I mean, if they start the process for both at the same time before any one results out, then you could eliminate on this bias. But these are the details that are best had in discussion with your reviewer.

**Rachel Liang:** Got it. OK, great. Thank you so much.

**Joseph Tartal:** Thank you. Our next question is from Ling Ko. I'm going to unmute now, so please unmute yourself and go from there.

**Ling Koh:** Hi, everyone. Thanks for taking my question today. I had a question about multi-analyte panel tests for SARS and flu. In the past, we've heard you say that these are recommended to be limited to prescription use rather than OTC since HCP involvement is generally needed to ensure the interpretation of the results is done correctly and that appropriate follow-up action is taken. Can you speak a bit more to where and how you envision that HCP would be involved? Are we talking about just them writing the prescription for the test? Or are we also talking about them actually being contacted or as part of the results interpretation stage?

**Tim Stenzel:** You can look at the home prescription tests that we've already authorized. There's still some on the FDA website. You can look at all the labeling, the IFU, the instructions, what we recommend. So it starts with a prescription written by the health care provider. And then the patient can get the test. And that may even be something that is done well before a patient has any symptoms or any need to test so that they have the test on hand.

When they complete the testing, then they're encouraged to report those results to their clinician and discuss those results with them. That's the additional mitigation that we're asking for in that situation. But again, I think we still have a couple that haven't moved to OTC in the home and that are prescription pills, so you can see the labeling and the interaction between patient and clinician that we recommend.

**Ling Koh:** So to clarify, even for a multi-analyte panel that tests for flu as well as SARS-CoV-2, we can leverage the same sort of recommendations for the test that does provide a flu exempt?

**Tim Stenzel:** Yes.

**Ling Koh:** OK, great. And just a quick follow up question-- if we were to conduct an extremely robust usability study and we actually showed that there was a high degree of results comprehension from the lay user regarding the differential diagnosis or diagnosis of both flu and SARS-CoV-2, could that potentially reopen a conversation about OTC and not just prescription use? Or that stance pretty firm at this point, that it has to be prescription use?

**Tim Stenzel:** Well, we always remain open-minded. But our concerns go to testing somebody who's asymptomatic for flu or RSV. We just don't know what that means in those two populations and what they should do with that information.

And so there could be false positives, could be true positives. And we just don't understand in an asymptomatic population, in particular, when we give an OTC authorization, it's typically a situation to use that for screening for SARS-CoV-2 given that there's so many asymptomatic positives out there.

And so the EUA authorities cover SARS. They don't necessarily cover any other analytes. We made some flexibility here to allow other analytes because they're certainly in the differential diagnosis if you have symptoms. But they wouldn't necessarily be in the differential diagnosis if you didn't have symptoms. And so if a patient is asymptomatic and gets a positive for flu or RSV, we want them to have a physician or clinician contact to try to understand what that means and know what to do with that.

**Ling Koh:** OK, and to clarify when you say physician contact, it doesn't necessarily mean that the result has to go through an HCP before being released, but that there is some method of contacting an HCP that is encouraged with the result?

**Tim Stenzel:** So it depends. I mean, there's home collection devices that physicians may want to look at the results before they release it to the patient. If it's a home test situation, the patients are going to see their results there before the physician or clinician does. And so we want to have there be a relationship between the patient and their health care provider established so that we know that that patient has access to a health care professional to help understand the results.

**Ling Koh:** OK, thank you. That's super helpful.

**Joseph Tartal:** With that, we'll take our next question from Julio Herrera. You are now unmuted. Please unmute your microphone and ask your question.

**Julio Herrera:** Yes, can you hear me?

**Joseph Tartal:** Yes.

**Julio Herrera:** All right, so I submitted this via email. And I guess it got missed or maybe it's for next week. So we're working on an at-home collection for serology assays. And so we're doing the clinical agreement section, which is the 30 unvaccinated and the 30 vaccinated confirmed infections.

My question is actually twofold. One is, for confirming positives, can we use an FDA EUA antigen or rapid test, such as the BinaxNOW, as a positive confirmatory test to basically include that as our positives?

The second question is related, but we've also had a number of individuals that we've collected that were vaccinated individuals and let's say are four to six months past their last dose of the vaccine that basically are now sending us a confirmatory positive result. Would those individuals be eligible as confirmed positives for this clinical agreement or for the usability?

**Tim Stenzel:** So I neglected to read a disclaimer at the beginning of the question that we went over that were received prior to the call. And this is true for every week. So we do receive some questions that are a little too detailed or test- or case-specific that we will not address on the call. And so I forgot to do that. So that was the case for your question.

So I do recommend that you reach out to FDA staff through the CDRH EUA Templates email address. Or if you already have a reviewer assigned, to reach out to them to engage them in this conversation. I'm not going to be able to go over that question today.

**Julio Herrera:** OK, all right. How long does it take them to respond? Because I sent in a question to them through that site several weeks ago and I haven't heard back from them yet.

**Tim Stenzel:** If it's been more than a couple of weeks, you can go ahead and send an another email to the Templates email address and ask them, in this case, to contact Toby.

**Julio Herrera:** All right, all right, thank you.

**Joseph Tartal:** Thank you. We'll go on to our next question. Tianyang Liu. I'm opening up your microphone so that you can unmute and ask your question.

**Tianyang Liu:** Thank you. So, hi, Tim. My question is that, is it more quick to submit pre-EUA and the EUA, or submit the EUA directly for the application?

**Tim Stenzel:** Can you say that again?

**Tianyang Liu:** There is two way, that we could submit the pre-EUA and then go to the EUA. Or we can also submit the EUA at the first. Which one do you recommend? Which one will be safe--

**Tim Stenzel:** Yeah, so for most EUA submissions today for routine sort of assay tests, we've got templates for all recommendations for all the studies. And there are lots of authorizations for all these common types of tests. So I really don't believe there's any need for pre-EUA and would not recommend that pre-EUAs be used in those circumstances, but that you go right ahead and do your EUA. And that will save a lot of time.

There is some risks, as always. But if you're doing exactly what others have done in the same manner, and according to our template, the risks are very, very small.

**Tianyang Liu:** OK, thank you very much, Dr. Tim. And one more question is that, if a submission-- I mean, if a protocol is really good, is it possible that it takes longer for your team to respond to review it? But once we receive the feedback, the official feedback, it will be really quick to proceed?

**Tim Stenzel:** So, we are still receiving so many applications and still have a backlog. And we're trying to get through everything. And again, it's why I don't recommend a pre-EUA if you're just fine with standard recommendations that the FDA makes for standard devices. People should reserve the pre-EUA for something novel, something new, something that we haven't discussed on this town hall, something that isn't in the templates, something there isn't a template for. That's where you get the most bang for the buck on the pre-EUA.

We do make some recommendations about pre-EUA. But that's not global and it's very specific and is trying to manage the workflow that we have.

So we have a lot of EUAs in house. And when we have an EUA in house, where perhaps all the studies were done and the tests can be authorized, it seems a little bit more important for us to review that than a pre-EUA for something that's very standard. But we're trying to get to all the work. It's just a lot of work.

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

**Joseph Tartal:** Our next question is from David States. I'm unmuting you so that you can unmute and ask your question.

**David States:** Hi. The EUA template for COVID diagnostics still indicates that saliva is regarded as an alternative specimen and asks for contemporaneously-collected swab and saliva samples for approval. There's an extensive body of literature that's emerged since then showing that saliva is a widely accepted and valid specimen for COVID diagnosis. And many EUAs have been approved on that basis. Can we now submit an EUA using just saliva specimens comparability for approval for COVID diagnosis? Thank you.

**Tim Stenzel:** You're not going to like my response. So we don't publish negative decisions. And we continue to see challenges with saliva tests. Saliva is an option that we provided. It's a very unique option in the world of respiratory viruses. Saliva-- we don't know, to say the performance of other virus detection-- flu, RSV. We've gotten questions about panels from saliva. And we just don't know if those viruses will work. We're open to seeing data.

But I've also seen data that suggests that the viral contents in some saliva patients can be much lower than a nasal swab or a nasopharyngeal swab. So our recommendations still stand for validation of saliva tests, that it gets compared to a nasopharyngeal swab.

**David States:** But a nasal turbinate swab would be acceptable comparison?

**Tim Stenzel:** We have allowed mid-turbinate swabs. That's correct.

**David States:** OK, all right. You're right, I don't like the answer. Thanks.

**Tim Stenzel:** Acknowledged.

Joseph Tartal: Let's go on to our next question. Franco Calderon. I'm going to unmute your mic. So please now unmute yourself and ask your question.

**Franco Calderon:** Thank you, Tim, it's been a while. So I'll begin with a comment. Perhaps, it's going to sound a bit of a rant, but you've heard this before. So there's been several publications here lately where people from very respectable institutions, like the Harvard School of Public Health, Johns Hopkins, and so on, have expressed their preoccupation with the fact that we still don't have enough rapid tests, such as rapid antigen tests. And they've alluded to how FDA treats these devices. And they've argued that this should be treated as public health devices rather than clinical diagnosis devices. I mean, this is something you heard over and over.

We submitted our application back in August 2020. And our issue has been not the performance of our rapid antigen test per se, because we've compared it to those that have EUA currently. We found that our test performs just as good or even better than the ones that are listed on the FDA.

Do you foresee-- our issue has been really the economics of getting our tests validated by the very few institutions that are able to do this kind of work in the US. Do you see FDA, CDC, NIH, or any organization like that playing a more active role in helping test developers like ourselves with the validation of the tests, like the UK has done, or several countries in Europe have done-- Germany to be a case, the UK another. Do you see that potentially being part of the program, I mean, now that the administration wants to increase the number of these kinds of tests to market?

**Tim Stenzel:** So thank you for your question. As I stated at the top of the call, antigen tests, very specifically I mentioned, if you were on the call at that time, continuing to be a top priority. And the FDA is doing its part to get through all the applications as quickly as possible and give feedback to submitters as quickly as possible.

Your idea of a US government stood-up program to evaluate antigen tests is an interesting one. Of course, the FDA and NCI and CDC stood up a program for the serology test developers. And I forget the latest number on serology tests, but we authorized almost 90, if not over 90 serology tests, many of them lateral flow devices very similar to antigen tests through that program.

And it's an interesting idea, and very willing to take that back. That program at the NCI was funded. And it took a lot of money to do that program. I don't know if the budget numbers are public. But I know the amount and it was not insignificant.

And obviously, I would be very supportive of something like that, because an independent assessment by the US government is quite valuable. And as we found out with the serology test, and I think I've mentioned this multiple times before on this call, those tests that were submitted to NCI and were cleared by the FDA to be tested at NCI, we did an initial review of all submissions only recommended to NCI those tests that after our initial review seemed important to test. So we did eliminate from the list before NCI tested, and still something like 60% to 70% of the tests that had passed that first FDA review failed at NCI. And so this kind of program can be very helpful for challenging questions. And I think it's a really good idea and definitely will take that back.

**Franco Calderon:** Thank you. And your example of the serology program is an excellent one, because it shows that it certainly can be done. And again, just going back to the fact that the Biden administration has increased funding to testing, rapid testing, OTC testing at home and over the counter.

But what I do see, though, is that a lot of those funds are going only to US-based companies. And while the approach looks great, but the truth is that there is a lot of bottlenecks, that these companies are not easily able to bring products to market, where test developers like us and many others, I'm sure, we have the products ready. I mean, these products are being sold elsewhere and they have demonstrated to be good.

So it would be great if you could take this idea-- I mean, it's not a novel idea-- back and maybe let us know if this is a possibility. Thank you.

**Tim Stenzel:** You're welcome. And thank you for the idea. And of course, for the serology lateral flow devices and some ELISA format serology devices that were able to be tested [AUDIO OUT] the US. So that's absolutely something that a program like this should consider.

And the other thing is I think the US government should consider novel approaches to purchasing and distributing tests outside of commercial channels. But that's not up for me, or nor do I think it's up to the FDA to decide. So I will take those ideas back. Thank you, and probably should move on to the next questioner.

**Joseph Tartal:** Thank you. And our next question is from Richard Montagna. I'm currently unmuting your microphone. So please unmute yourself and ask your question.

**Richard Montagna:** Well, thank you. And I guess let me apologize up front. This is probably a redundant question addressing what, Tim, you indicated at the top of the call regarding changes to an existing EUA test.

We have a molecular PCR-based assay that's been authorized. And we're currently evaluating changes that will decrease the time that it takes, thereby increasing the throughput of the platform. Am I correct in understanding that once we are satisfied we're getting the performance that it would be equivalent to the current authorized test, we can implement that with high complexity CLIA labs while the EUA is under review? And I'm assuming that when we send in the EUA in our cover letter, we will indicate that we are going to immediately implement, that they're basically software changes. So wonder if you could just clarify that for me. Thank you.

**Tim Stenzel:** Yes, do read the policy guidance on this and adhere to the provisions, which I think there's a certain amount of time after you've validated the modification. I think it's a similar timeline as if you validate an entirely new device, and then the amount of time before you send it in.

I think with commercial devices-- and Toby, if you're still on-- that submission has to be made, but you don't have to wait on the review of the change or the device prior to launching that. Toby--

**Toby Lowe:** Right.

**Tim Stenzel:** I forget the exact timing.

**Toby Lowe:** That's right. For modifications to a commercial diagnostic COVID test, once you've submitted your amendment to request authorization for the modification, you can implement that in high complexity labs.

**Richard Montagna:** OK, thank you very much. I appreciate that.

**Toby Lowe:** Yep.

**Tim Stenzel:** Fantastic, thanks.

**Joseph Tartal:** Our next question is from Kelli. I just unmuted your mic. So please unmute yourself and ask your question.

**Kelli:** Hello, thanks for taking my call. I appreciate that I have received consistent information from these town halls. And I had some questions.

So as an antigen test developer, you have consistently stated that for multiplex devices, developers should align with FDA on how they are going to validate the test especially in the absence of, like, for example, influenza prospective samples. I have submitted questions to the CDRH Templates' website, or the email box, and a pre-EUA. And in the absence of having feedback from FDA, what do you recommend as to a way or a path forward to proceed to with the submission?

**Tim Stenzel:** If that's been more than a couple of weeks since you submitted your pre-EUA, please send it back to the Templates email and ask please ask for Toby to get connected to find out if we can give you even more specifics about your submission.

But this is a challenge. So particularly with antigen devices, bank samples can be challenging if they're not banked direct swabs. And people just don't typically bank direct swabs.

And so we've seen so many issues with antigen tests. And we've removed VTM from a number of antigen test authorizations for this pandemic because of the issues we've seen with VTM. VTM can raise the baseline, artificially increase the sensitivity of device, and then raise the false positive rate. So that we're really not pleased with VTM.

So this is a really, really challenging question, because we have so many already fully authorized flu point-of-care and central molecular tests for flu. And the flu is not the pandemic virus-- the pandemic virus that gives us authorities, some of the EUA processes for SARS-CoV-2, COVID. But we've tried to be as flexible as possible and stretch those authorities as far as possible and to help out here.

The good thing is there's not any flu now and there may not be any flu this season. So that the other thing that we've consistently messaged is, if you're not able to get validation done for the non-SARS targets on your device due to the fact that you can't get appropriate bank samples, and you can't get those positives prospectively that are fresh, look at how you can somehow turn off the results for those other analytes that you don't have enough positives to get an authorization for.

And sometimes that's more challenging, say, for a non-instrumented- or non-smartphone-read rapid antigen test because it's a visual read. And your top cassette may say flu A for the SARS on it, but we'll

be imaginative and creative in what you can do in that situation. For example, if the window is too big for SARS because the home user might or the point-of-care user might see the flu bands and get confused, then they can make that window smaller. You may be able to remove identifiers from those extra bands if people will not be confused by those extra bands.

If it's a smartphone reader or instrumented device, you can simply turn off the reporting from those bands until those are authorized. So you can get an initial authorization for SARS only. And then once you accumulate enough data and can submit the additional data for the additional targets, those things can be turned on, physically or electronically, whatever is the possible way.

So that's what we've done for prior devices prior to the pandemic. And BioFire is a great example where they have this huge panel of respiratory viruses and sometimes other panels. And they may or may not get enough data for the less common targets. But they go ahead and get authorization for what they can get at the time, and then they update their submission and expand their authorization.

So trying to be as flexible as possible. At the end of the day, we need to know if these flu or other non-SARS targets actually work so that patients are getting accurate information.

**Kelli:** Right, I appreciate the information. When I submit again, do I just ask that the information gets forwarded to Toby.

**Tim Stenzel:** Correct.

**Kelli:** OK. And then I had one other question, and this is just real quick. The transcripts have not been posted for a while. Can you give me some information regarding when I can expect to see some of the more recent transcripts posted?

**Tim Stenzel:** Joe, can you address that question?

**Joseph Tartal:** So I can speak to that. I actually have a couple of the transcripts in hand right now. I'm hoping to get them posted by Monday to at least catch us up through to the last town hall. And I'm working towards getting that one together as well. So I apologize that we are a little bit behind on the transcripts. We are working to get that addressed and get them posted as soon as possible.

**Kelli:** OK. And then just submit everything as-is and explain?

**Tim Stenzel:** Yeah, yeah.

**Kelli:** OK, perfect.

**Tim Stenzel:** Or just provide your pre-EUA number.

**Kelli:** OK, perfect.

**Tim Stenzel:** And. ask that Toby give it, and then Toby can look at it. All right.

**Kelli:** Thank you so much.

**Tim Stenzel:** We have a couple more.

**Joseph Tartal:** Yep, so unmuting Samantha Eakes. Please unmute your mic and ask your question.

**Samantha Eakes:** Hi, thank you so much for taking my question. And thank you, again, for all the hard work you've been putting into these town halls and to COVID in general.

I just had a question about the notification pathways. I know that the one for diagnostics for PCR and antigen has been continued to be updated. And the antibody one for manufacturers hasn't been updated for a few months. Are those still viable pathways for manufacturers to use in order to market to high complexity while they're waiting for their EUA? Thank you.

**Tim Stenzel:** The notification pathways as spelled out in the current guidance are still open. I was not aware perhaps that some devices weren't showing up timely in the notification page. If that's the case, then that those developers should just reach out to the FDA and ask. Sometimes we don't require that notification to be posted, but I think for all commercial manufacturers we do.

All right, let's move on to the next questioner, get as many people in.

**Joseph Tartal:** I'm muting Lee Young. Lee, please ask your question. Lee, if you're there, please unmute yourself and ask your question. I'm going to move on to Mary Ann. Mary Ann, I'm unmuting your line. Please ask your question. Unmute yourself and ask your question.

**Mary Ann:** Hi, good afternoon. Can you hear me?

**Joseph Tartal:** Yes.

**Tim Stenzel:** Yes.

**Mary Ann:** OK, good. In a clinical trial for a multi-analyte antigen detection test-- that is, flu plus SARS-- if a reference RT-PCR assay does not have claims for a specific specimen type, but the reference laboratory we're using has validated that specimen type, is it acceptable to use the results from that lab-validated specimen as a reference? Thank you.

**Tim Stenzel:** If it's modifications to an EUA test and the FDA hasn't reviewed and authorized those modifications, that's a challenge. If it's a fully cleared device and modifications have been made that haven't been FDA authorized, that is a challenge. We're not going to say no. But basically the modifications to the test would have to be reviewed and found to be authorizable, at the very least, in order for us to accept that data.

So then you're asking our review team to not-- and actually, if it's an antigen test, then the antigen team would be reviewing the antigen test, and the molecular team would be reviewing the modifications to a molecular test. So that's just terribly inefficient. So that's why we do recommend that you use fully EUA-authorized methods that are acceptable as a comparator.

Those are high sensitivity molecular tests. Or you can use a fully cleared or authorized molecular test without LDT modification. That's our recommendation. Once they know how to do it, but it will really muck up the system more than needed.

**Mary Ann:** OK, thank you, thank you. I think that's generally a no.

**Tim Stenzel:** It's not a no. It's not a recommendation.

**Mary Ann:** OK, thank you, thank you.

**Joseph Tartal:** With that, Tim, do you have time for one last question?

**Tim Stenzel:** Let's take one more, if we can actually--

**Joseph Tartal:** This will be the last one.

**Tim Stenzel:** We can.

**Joseph Tartal:** So again, I'm unmuting you. Lee Young, please ask your question.

**Lee Young:** Fantastic. Thanks, Joe. Can hear me?

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

**Tim Stenzel:** Sorry about that. I don't know what happened the last time.

**Lee Young:** Tim and Joe, thank you for the time today. For a test developer pursuing a 510(k) with the SARS-CoV-2 assay, we're trying to use anterior nares samples. But the only on market 510(k) cleared assay is the Biofire. And it uses a nasopharyngeal swab.

Which would you recommend? Would you recommend validating a nasal swab on the Biofire assay before using it as a comparator method? Or would you instead use an EUA-authorized assay that uses nasal swab, and why?

**Tim Stenzel:** So whatever you use, we recommend you use either a fully authorized method, including the sample type, or an EUA-authorized method, including the sample type. You choose. It doesn't matter to us which you use as a comparator, as long as it's an acceptable comparator, a high sensitivity molecular assay.

**Lee Young:** OK, thank you.

**Tim Stenzel:** All right.

**Joseph Tartal:** With that, that was our last question.

**Tim Stenzel:** I think we're done.

**Joseph Tartal:** Yep. So thank you, everyone. We greatly appreciate your participation today. The 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). Note that we've updated the title of the section to make it easier to navigate.

You'll find the recording and the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. And as was noted out throughout the program today, for additional questions about today's presentations and topics for COVID-2 testing, 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 may find at [www.fda.gov/CDRHWebinar](http://www.fda.gov/CDRHWebinar). Last as a reminder, please join us for the next webinar on October 6.

With this, it concludes today's town hall. Thank you.

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