Virtual Town Hall 8-18-21

Moderator: Anike Freeman
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Anike Freeman: Good afternoon and thank you for joining us today. My name is Anike Freeman, a Senior Consumer Safety Officer in the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. I'll be moderating today's program.
I'd like to welcome you to our virtual town hall meeting for SARS-CoV-2 test developers. This is meeting number 67 in our series in which we'll discuss and answer your questions about diagnostic tests in the fight against COVID. 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, Associate Director also from OIR.

First, we will have opening remarks from our speakers. And then we'll begin answering your questions about the development and validation of COVID tests. To ask a question, please select the Raise Your Hand icon at the bottom of your screen. Please note we're not able to discuss specific submissions that are under review. Now, I'll hand the program over to Tim.

Tim Stenzel: Welcome, everyone. I believe this is the 67th CDRH virtual town hall meeting to assist all of you test developers in developing tests to meet current pandemic needs. And, just to reiterate, our priorities have not changed. We continue to prioritize access to high-volume testing nationwide, particularly for diagnostic tests, so point-of-care diagnostic tests, home diagnostic tests, high-volume central lab tests, and diagnostic home collection. So those are the priorities for, I presume, obvious reasons. And we continue those.

One second because Toby wanted me to mention something, and I'm not finding that. Toby, do you want to make that statement? I'm not finding what you wanted.

Toby Lowe: Sure. Yeah, it's part of the discussion on priorities. I know we've had a lot of questions recently about multianalyte tests. So I just wanted to clarify that we are accepting and prioritizing prescription multianalyte tests, but not over-the-counter.

Tim Stenzel: Thank you, Toby. And, with that, I think we can move over to the few questions that we received ahead of the call. And over to you, Toby.

Toby Lowe: Great. Thanks, Tim. And welcome, everyone. So, as I have mentioned on previous calls, we do sometimes receive questions that are too detailed or case specific to address on this call. For those, we do try to send a response in writing within a few days. So, if you've submitted a question and don't hear it addressed on the call today, please keep an eye out for a written response. And, if you don't receive one within a few days, please reach back out to the CDRH-EUA-Templates@fda.hhs.gov mailbox for an update.

So we do have one question that we received ahead of time today that we'll address regarding an antigen test for SARS-CoV-2. And there are two related questions here. The first is asking about what review pathway FDA recommends, whether the EUA review pathway or the traditional, premarket review pathway.

And, similar to what we've said on previous calls about both molecular and antigen tests, for tests that will most benefit the current public health needs, EUA does remain the fastest and least burdensome route to authorization. Sponsors interested in pursuing full marketing authorization through a de novo or a 510(K) are also welcomed to do so.

And then the second part of this question is asking about what additional clinical performance requirements would be in place for traditional premarket review pathways, such as 510(K) or de novo, compared with an EUA request and, specifically, with respect to clinical performance data, asking whether both prospective and retrospective studies are required if the developer plans to use the traditional premarket review pathway.

So, since we've not yet authorized an antigen SARS-CoV-2 test for full marketing yet, we would generally recommend a pre-submission. Typically, for full marketing authorization, we're likely to expect a higher-powered, prospective clinical study, so more positive than negative, than what we would expect to support an EUA, as well as analytical studies of course.

And, while it is specific to molecular, the decision summary for the SARS-CoV-2 BioFire de novo, which is the only SARS-CoV-2 test that has received full marketing authorization at this time, might give some insight into FDA's thinking about what we're looking for full marketing

authorization. And, with that, Tim, I can pass it back to you unless we have any hands raised for questions at this time.

Tim Stenzel: It doesn't-- if my dashboard is correct, we're not seeing any hands raised at the moment. Oh, there's one. Now they're coming in. So let's go ahead and look to that. Thank you.

Anike Freeman: Alright, our first question will be from John Mann.

John Mann: Yes, I know that you're prioritizing the high-volume testing, point-of-care, home diagnostic, diagnostic home collection. If you have a CLIA lab-based EUA, one, are you still accepting those? And, two, what would be the expected turnaround or response time for those?

Tim Stenzel: So can you tell me a little bit more about the CLIA lab test? Is it all performed within one lab, and you get health care providers submitting samples directly to you? Is that sort of the scale of things?

John Mann: Yeah, it would either-- it would be a collection from either home or clinician. And they would-- it's a molecular test. It would be submitted to a single CLIA lab.

Tim Stenzel: Yeah, so home collection is considered a device. And we do require review of that. And so, if you have an LDT that wants to add home collection, then we look forward to getting the submission and working with you. If it's a standard LDT and it doesn't involve, say, home collection or some other device-related issue, we are still in discussions with HHS on LDTs. Toby, do you want to add anything else?

John Mann: Yeah, this would be performed in a CLIA lab. So, if we do it in a CLIA lab, do we still need to submit it through the EUA?

Tim Stenzel: If you do home collection, yes.

John Mann: No, if you did it just with, let's say, from clinics.

Toby Lowe: So I think--

Tim Stenzel: If you're just accepting-- go ahead, Toby.

Toby Lowe: So are you-- is this a single CLIA lab and that you're developing the test in that lab with an LDT? Or is it a collection-- or sorry, a test kit for use in a CLIA lab?

John Mann: It would be a test kit that is used-- that is sent to the CLIA lab from either point of care or from home.

Toby Lowe: OK, so then it is-- it would need an EUA. Yeah, if it is a-- if it is a test that is developed and used solely in a single lab-- so it's a lab-developed test that does not have home collection-- then that is something that is still under discussion with HHS regarding the statement they issued last summer about LDTs.

Tim Stenzel: Yeah, I might have heard incorrectly. But I thought John said this was a kit that's purchased from a developer that probably has an EUA. You want to run that in the CLIA lab, but you want to add home collection to it. John, could you please clarify the question?

John Mann: So this would be a developer who's developing a test. It would be performed in a CLIA lab. And let's assume it's only at point of care.

Toby Lowe: Right, so, for that, we would expect to see an EUA request for that.

Tim Stenzel: You know, what I recommend, I can imagine some scenarios where we've given guidance in the past that complicates this answer. So I wonder, John, if you wouldn't mind sending an email to our templates email address and ask to be connected with f and Tim. And we'll find out a little bit more details and give you a little bit more directed feedback. And, if it comes to us, we'll do that rapidly, OK?

John Mann: Very good. Thank you so much. I appreciate it.

Anike Freeman: Alright, our next question is from Jeanna McLeod. Jeanna, are you there?

Tim Stenzel: Jeanna, still can't hear you.

Anike Freeman: OK, we'll try to come back to Gina. Our next question will be from Ron Domingo.

Tim Stenzel: It looks like Ron is muted.

Ron Domingo: Hello. Tim, can you hear me?

Tim Stenzel: Yes.

Ron Domingo: OK, perfect. So we're working with the company on a total antibody test. And they are currently recruiting subjects into the clinical trial. We know from the template that the sample size is 30 positive and 75 negative samples.
However, it's likely that we're going to encounter both vaccinated and unvaccinated individuals in our recruitment. Does this change the sample size considerations? Or does FDA have a recommendation on the distribution of positives and negatives required if we were to include both?

Tim Stenzel: So, for the positives, you know, vaccinated individuals would present a challenge for total antibody tests because the spike protein will be detected. And you won't know if you're detecting post-vaccination or post-infection.

Unfortunately, there is a huge percentage of those in the US now who are not vaccinated and who are acquiring COVID infection. And so it really shouldn't be a challenge to get 30 positives. The 30 that are not vaccine-- or are vaccine naive. The negatives, as we increase the numbers of US citizens who are-- or folks in the US who are either vaccinated and/or post-infection, the latest estimates I've seen is that somewhere just shy of 10% of those in the US-- and I think numerous publications, high-quality publications, note this is somewhere shy of 10% have been infected in the US based on seroprevalence. And then, of course, somewhere around 50% of the people in the US have gotten somewhere around one vaccine at least. So that unfortunately leaves about somewhere around 40% of the folks who are both vaccine naive and potentially have not been infected.

You can also use pre-pandemic banked negative samples for the negative pool. Don't know how pre-pandemic banks are doing as far as available volumes to provide to test developers, but that's certainly an option.

I see that serology test developers will be having an increasing challenge to find true negative, let's say, fresh samples, during the pandemic samples. And, when you run into those sort of problems, just chat with our review staff. You know, eventually, we are likely to have to move to a different comparator method establishing, initially, probably sooner on the negative side and then, eventually, potentially on the positive side, as we unfortunately move to 100% either post-infection and/or post-vaccination population. But, for right now, we think it's still doable. The numbers are relatively small at 30 and 75. Hopefully, that's helpful. But we need to move on because we do have a number of callers.

Ron Domingo: Alright, thank you.

Anike Freeman: OK, we're going to come back to Jeanna McLeod.

Tim Stenzel: Hey, Jeanna? I can't hear you. We have another raised hand, so let's kind of move down the list now if we could.

Anike Freeman: Our next question will be from Tianyang Liu.

Tianyang Liu: Hello. Hello. Thank you very much, sir. So my question is regarding one question that was raised in previous town hall meeting last week. In the town hall meeting, there is a question about clinical evaluation of OTC home-use antigen that can be interpreted either visually using the paper guide instructions or using a smartphone app. And the question is asking whether a certain number of certain positives have to come from participants using paper versus the app.

And I recall that, during last meeting, you replied that FDA expected to see 30 positive and 30 negatives for visual interpretation and another 30 positive and 30 negative for the app interpretation. Am I right?

Tim Stenzel: That is correct, yeah.

Tianyang Liu: And then so there is-- so this is my question. What does it mean by interpreted using a smartphone app? If the user read visually a test card and just inputs the result manually on the smartphone, I think it has not been interpreted by using a smartphone app, right? I guess,

interpreted by a smartphone may mean that the patients take a photo by the app, and the app interprets the photo, and it represents a result, test result, automatically.

Tim Stenzel: Yeah. So, when we talk about a smartphone app interpreting the test, it's not recording. It's not having the patient record the result on the smartphone manually. It's you have a camera function. And you have a camera function, and the camera records an image. And it is image analysis, and the smartphone image analysis is deciding whether the test is positive or negative.

It's when the smartphone is doing all of that that we need to see a separate 30 positive and 30 negative in the OTC environment. But, if all of the smartphone is doing is having the patient record the result that they visually read, that is part of the user testing and the clinical study. And you don't need to have a separate study to analyze that.

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

Tim Stenzel: Uh huh.

Anike Freeman: Alright, our next question is from Tom Hayhurst.

Tom Hayhurst: Yes, I have a question very similar to the one that John Mann asked in the very first question. As far as the collection, I understand an NP and even a cheek swab as a device. But what happens for a blood spot that is collected, well, let's say, in the home setting and sent through the mail? If that could be validated in terms of sensitivity and specificity, can the lab director sign off on a sample collected in that manner?

Tim Stenzel: The short answer is no. We consider that a medical device and outside the purview of an LDT.

Tom Hayhurst: OK, thanks.

Tim Stenzel: Mhm.

Anike Freeman: Alright, our next question is from Ela.

Ela: Hi, my question is about a saliva COVID test intended for the CLIA setting with freshly collected saliva. So, for the analytic studies like determining the LoD, the template asks to use real clinical matrix, which, in this case, ideally, would be fresh saliva, which is a little bit tricky. So my question is, would it be acceptable to use artificial saliva or another commercial source of saliva where the saliva won't be fresh? Or do we have to use freshly collected saliva?

Tim Stenzel: Yeah, that's a really specific question. And I think it's best to work with our review staff. So artificial saliva, no, that's not going to be acceptable. We see saliva continuing to be a very challenging sample type.

Some recent publications imply that the viral levels can be lower, and shedding can be for shorter periods of time. I don't know what the truth is, other than we have directly observed that there's some challenges with saliva. And that doesn't allow us to authorize that sample type. So it needs to be real. Potentially, frozen banked could be used, but, in all likelihood, we'd ask you to do a fresh/frozen study to make sure that freezing the sample neither degrades or frees up additional virus and might artificially increase the sensitivity of the test. So, potentially, it's OK, but I think that's a detailed enough question, best left to our front-line review staff to help you out. Hopefully, that's somewhat helpful to you.

Ela: OK, so I can just send an email and ask that specific question?

Tim Stenzel: Yes. They may want to know more about your assay. And it may be best to be in the context of a pre-EUA. And, therefore, you can just frame the topic as saying, this is what you would like to do. This is our test. And, yes/no, is this acceptable?

Ela: OK, thank you.

Anike Freeman: Alright, our next question is from Jack Feng.

Jack Feng: Hello. Can you hear me?

Tim Stenzel: Yes, welcome.

Jack Feng: Good morning, sir. So it is still morning because I'm living in California. And my question is about our app too, our mobile app too. So we submit our EUA for antigen test two

months ago, currently still under review. And, recently, we noticed that the school is reopening, and it's quite a mess because my kids is going back to school too. The school cannot handle this kind of situation.

So we quickly developed new features for our mobile app, which can help schools to better organize the students and also manage the test results. But our concern is that, if we update our app right now and submit to the FDA, it will be slowed down the review progress because we submit our application two months ago. So I hope that is already in the end of the review. So we don't know, if we update our app to help the school reopening, how much it will slow down our review process. That's our--

Tim Stenzel: It depends. It depends on the change. If the change affects the performance of the app reading of the antigen test result, then we may have to restart our review on the clinical and analytical studies. So, if you send an email to the templates email address box and ask for Toby and Tim, they'll forward it to us, and we'll check in on your application and provide you a little bit more--

Jack Feng: Alright, thank you.

Tim Stenzel: --direct feedback on the situation. In the email, if you can say what the changes are to your app and what the potential impact is on test results, then that will help us more quickly get you a response.

Jack Feng: Alright, thank you.

Anike Freeman: OK, our next question is from Dana Hummel.

Dana Hummel: Hi, can you hear me?

Tim Stenzel: Yeah. Hello, Dana.

Dana Hummel: OK, thank you. I have a follow-up question related to the questions regarding a home collection device for a lab-developed molecular test. So would a home collection kit for a nasal swab specimen qualify as part of the LDT, which is a PCR test, or would it require an EUA? This would not be commercially sold and would only be used by this particular lab.

Tim Stenzel: Yes, it requires an EUA. Typically, all home collections, for something that hasn't already been FDA authorized for that specific purpose or hasn't already received an EUA for that specific purpose and you're just using it within all the conditions of the use of that home collection device, we're going to want you to come in and explain what you're doing. But, by and large, the vast majority, if not all of these, are considered devices and subject to FDA review.

Dana Hummel: OK, thank you.

Anike Freeman: Our next question comes from Robert.

Robert: Hi. Hello, can you hear me? This is Robert Di Tullio.

Tim Stenzel: Yes, hi, Robert.

Robert: Hi, Tim and Toby. And thanks for taking my question. My question is surrounding the recent news of the CDC data showing an ebbing in vaccine efficacy that's prompted the White House to recommend boosters after eight months or what have you. That suggests to me that the assessments of immunity gains more importance. So I was wondering what FDA's view of the importance and priority of antibody testing and immunity assessment has changed in light of this.

Tim Stenzel: Yeah, so there's more than a dozen ongoing clinical trials of immunity determination, all on ClinicalTrials.gov, that we're monitoring. The FDA is not running them. And we're looking forward to seeing the results of that before we look to offer pathways to seek-- clear pathways to seek immunity or protection claims for serology tests.

If we look at other situations where the FDA has authorized serology tests for this sort of purpose, rubella is a really good example. There is a fully quantitative rubella serology tests traceable to international standard so that all the tests are in agreement when you get IUs per mL. And all the longitudinal studies have helped us understand-- helped all of us understand what a sterilizing level of antibodies are for rubella. So you know precise cutoffs above and below which you make clinical decisions about.

That was the hope for SARS-CoV-2. And we are still looking forward to seeing the results of those outcomes studies. And, if they're able to define such a level that can be traceable to an international standard, in all likelihood, a fully quantitative test may be needed.

Then we will move forward. And, any device that's already authorized and can meet that standard, we will update-- very willing to update their authorization without them, those developers, having to do their own outcome studies. We will not-- because we can link-- if we can link things to an international standard, then it takes away the need for all the separate serology devices that may be able to meet the need to have to do their own outcome studies. That would be very-- that would not be in the best interests of public health.

However, I do want to caution listeners that we don't do serology testing for some viruses, for example, for flu. And there is a reason for that. And, due to the variants, which occasionally now appear to have breakthrough infections, even in fully vaccinated people, like Delta, it's quite clear that, when you take into account variants and mutations, that there are differing levels of-- when you measure neutralizing ability, different levels, whether you got vaccinated, or you have natural infection and what variant you got natural infection from.

And then, when you look at other variants, what is the neutralizing level of antibody? And they're not-- the current data, my read of the current data-- and it's just my read-- but our team of serology experts at the FDA has been examining this and keeping track of this. So we're seeing concerning signs that it may be challenging to define a precise and accurate level of immunity or protection that would cover potentially all scenarios, whatever you were infected with or whatever you were vaccinated with and then all the current circulating mutations and vaccines. So I'm just urging caution here. We will be driven by the results of data. And, if the data supports it, the FDA will absolutely support those claims in the manner that I addressed.

Robert: Thank you for that answer. That was very thorough. Can I have a very quick follow up please, Tim?

Tim Stenzel: Sure. But we do have a number of callers that we [INAUDIBLE].

Robert: So, after my second dose of Moderna, I took a semi-quantitative test. And my titer was off the charts. And now I'm wondering, is the eight months applicable to me? Is it applicable

across the board? Is it just a suggestion? And, if so, wouldn't it be good if I were able to find out where I sit on the titer range?

Tim Stenzel: Yeah, as I said on our recent national call with infectious disease docs and clinicians, you know, I think we're looking at not who shouldn't get vaccinated, but rather who should be vaccinated and/or get a booster. The feeling that I'm getting-- and this is a feeling, and it's a gestalt of all the literature I'm reading-- is that we're moving towards a recommendation at the public health level, and it's not my decision, but more like flu, which you're supposed to get an annual flu vaccine.

But, again, I'm not speaking for the FDA or the vaccine group here. I'm addressing the question of the utility and clinical validity of using serology tests here. And I will say that the benefit/risk for serology testing, as just sort of espoused by you and others that I've talked to, we don't want serology tests to be misused. And we don't want the wrong interpretations to be made on the basis of a serology test because, as I said, it's very complex.

How did you gain an antibody response specifically? And have we done all of the work to find what it means for you down to the individual? I mean, population studies are one thing. And getting a p-value of less than 0.05 is one thing. But knowing what to give you as a patient, a specific recommendation, that's really what the FDA is focused on, not on population studies. We look at what is the best way to inform individual patients of their health.
So to be honest, it's very complex. And we're very open to it. And I'm giving you my personal, not FDA, speak here on vaccines. And I don't want to confuse that. I really want to make sure that's in the transcript.

That's just kind of the way we're looking at it. And, when I'm reading what others are recommending, I think that's what they're saying, but, again, and that's why they're making this recommendation probably for eight months to get boosters after your first vaccination. Alright, let's move on. Thank you.

Anike Freeman: Alright, our next question is from DBrinza.

DBrinza: Hi, just checking my volume. Can you hear me?

Tim Stenzel: Yes.

DBrinza: OK, thank you. This is a question regarding the serology template and the control-- well, the comparator for clinical evaluation. I know that, right now, the template lists out that there isn't an exact method for a comparator so that FDA is authorizing the RT-PCR comparator test.

My question is, would you be utilizing the RT-PCR to screen and enroll for the serology clinical testing people who are positive at t equals 0, I guess I would say, at their initial visit? And then would you also-- because it's a nasopharyngeal test versus a serum test when you're doing like a lateral flow IgG or IgM test, would you also then be having the patients undergo those nasal samplings at, say, day 14 or day 7 or day 15 after their initial test as well if you do a follow-on visit? So are you asking them to do a blood test as well as a nasal swab?

Tim Stenzel: So we want the RT-PCR test to establish the closest thing to truth about whether that patient was infected or not with SARS-CoV-2. And then we're looking at the day after symptoms and/or after the molecular test to look at how soon is the test, the serology test, able to detect an antibody response to that infection.

And then we list performance, as you've seen in all the prior authorizations, by days after ranges. And we really want to see that, in the two to three week range, performance achieves expectations as far as sensitivity and while maintaining adequate specificity. Hopefully, that addressed your question.

DBrinza: Yeah, that does actually. Thank you so much.

Tim Stenzel: You're welcome. OK, let's move on to the next caller, please.

Anike Freeman: I'll go back to Jeanna McLeod who has another question.

Jeanna McLeod: Hello, can you hear me now?

Tim Stenzel: Yes, hello, Jeanna. We've tried a couple of times. Welcome.

Jeanna McLeod: Ah, yes. I dialed in by phone eventually. Thank you for your patience and coming back to me. So we're developing a multianalyte antigen test. And it's based on a

qualitative influenza A/B point-of-care test that was cleared by FDA in 2020. So, when we're looking at selecting a cleared flu method to serve as a comparator for the multianalyte test, does the FDA have any general limitations or considerations or recommendations on selecting that comparator?

Tim Stenzel: If it's for viruses other than SARS-CoV-2, previously cleared or granted flu and other virus tests are fine for the comparator. We do not make any additional recommendations for that.

Jeanna McLeod: OK, that's perfect. Thank you.

Tim Stenzel: Uh huh, you're welcome.

Anike Freeman: Alright, we'll go to Tianyang Liu for a second question.

Tianyang Liu: Can you hear me?

Tim Stenzel: Yes.

Tianyang Liu: Thank you, sir. So my question is that we all know that the app will be updated frequently. For the app of the product already getting EUA, is it necessary to do EUA update for all the app changes, especially the changes--

Tim Stenzel: It depends. Go ahead. Go ahead.

Tianyang Liu: --especially the changes that do not involve the operation and use of the kit and do not affect the safety and effectiveness?

Tim Stenzel: Yeah, so, if it doesn't affect the performance, the sensitivity, specificity, usability of the test, then we're unlikely to ask for any data. But I would bring that up in the initial review process of your test and address that question with our front-line review staff. And they can give you a more detailed response on when they would like to see an amendment or supplement and when they don't need to see it or when they just want to get a notification or something, OK?

Tianyang Liu: OK, thank you very much.

Anike Freeman: OK, let's try to go back to Raouf Guirguis again.

Raouf Guirguis: I guess you can hear me now. Can you hear me now?

Tim Stenzel: Yes. Yes, I can.

Raouf Guirguis: Two questions, Tim. One is policing the serial testing because people may misinterpret that and do it once instead of twice to report the positives. And then, the second one, anything the FDA is doing on the post-COVID-19 syndrome?

Tim Stenzel: Ah, OK, yes, two questions. So, unfortunately or maybe fortunately, we don't have the resources to check that home OTC users are doing serial testing. That's how the devices are labeled, and that's how we want them to test.
But there's really-- we don't expect the manufacturers to ensure that their users are following that. What we expect is that the labeling is good, instructs them on what to do, and then we understand that, when things go to an OTC environment, that they could be used in all sorts of different ways. And that is a risk of OTC when a clinician is not involved. And it's why really the FDA is a lot more cautious in authorizing OTCs.
Now, obviously, we've done it numerous times, but those are the-- when we do our likely benefit to likely risk calculations for every EUA, for OTC, that goes into the hopper. And we compute that at least with brain power.

Raouf Guirguis: OK, second question was about the post-COVID syndrome. We're seeing a lot of cases now, several side effects. Is there anything the FDA is doing in terms of helping the clinicians diagnosing these cases or monitoring these cases?

Tim Stenzel: So we know that at least some of these cases did not have an original documented diagnostic test confirmation of COVID with, say, an antigen test or an RT-PCR test. And so clinicians are seeing symptoms of an overactive immune system. And they look at various biomarkers that are on the market to assess that.
As part of that workup, we understand that those clinicians are using a serology test to confirm whether or not those individuals have had prior exposure to SARS-CoV-2 and developed an antibody response. So that can be very helpful in the assessment of those kids.

And, certainly, there is interest in developers. And we've had ongoing conversations about additional tests that may help assess whether or not it is long COVID in kids or in others or not. And so the FDA is committed to taking a look at those ideas and those applications and assessing them for their benefit/risk in this pandemic response.

So they really-- it's not something that we can easily come up with a template and a set of recommendations for because these technologies really are all over the map in ideas. And so it's not something like, we know what the virus is, and we're going to detect it with molecular means, antigen means, or serology means. Those are a lot more standard sort of ways to assess infection or prior infection.

And so we take these one off. We assess them one by one. And, certainly, as I said, we would be open to assessing these technologies for their benefit in the pandemic response. Hopefully, that addresses your question.

Raouf Guirguis: Very helpful, thank you.

Anike Freeman: Alright, we have a question from FM2601@gmail. Please unmute. Alright, we'll move to the next question, which is our last in the series. We'll go to Sean Gregory.

Sean Gregory: Hi, a quick question regarding, for manufacturers looking to develop a respiratory panel for molecular tests, the BioFire Respiratory Panel 2.1 was recently approved. For developers looking to receive approval, would they only require the-- would the FDA only require to BioFire 2.1 as a comparator? Or will there still be required two additional EUA-approved or additional FDA-approved devices as a comparator?

Tim Stenzel: Yeah, for the 510(K) pathway follow-on molecular assays that can follow that reg, the BioFire assay is the formal predicate device. That does not mean that it has to be the comparator. And Toby, I know you're a little bit more fluent in this. And maybe I can have you finish our response.

Toby Lowe: Sure. Yeah, so we have discussed this on this call previously, although it would probably be several weeks back if you wanted to go look at the transcript. But yeah, we have talked about this that BioFire is the formal predicate, as it is the only test that is legally marketed

beyond an EUA. But you can still use other EUA-authorized tests as your comparator since we know that BioFire may not be available to all developers as a comparator.

Sean Gregory: OK, thank you.

Tim Stenzel: Sure.

Anike Freeman: Alright, and one last question. FM2601, let's see if you can connect this time.

FFIM2601@gmail.com: Two questions.

Tim Stenzel: Hello, I can hear you.

FFIM2601@gmail.com: OK, two questions, the first question is, is there a viral load serology test, viral load with the blood like you would in HIV, being developed for people who have long-term symptoms or to see ways of lowering the viral load for long-haulers? And can you tell the difference between a natural infection and a vaccination in terms of serology, like neutralization antibodies versus spike protein antibodies?

Tim Stenzel: So I'll take the second question first. Yes, we put out some communication. Toby can correct me here. So clinicians can definitely use the appropriate serology test or tests to assess whether just spike protein antibodies have been formed versus some other part of the virus that other assays, but the vaccines don't target.

So, obviously, positive on spike protein and negative on, say, N protein would suggest vaccination only. But, if you were to also see and confirm N protein antibodies as well, then it would suggest that there had been a natural infection plus or minus vaccine.
Regarding a viral load, the level of antibodies, we don't know if it corresponds to the viral loads that we're seeing in the patient versus maybe more patient-specific immune responses. But I'm not sure exactly what your question is. But we also know that there are developers out there who are working on blood-based detection of the virus, viral infection.

So it's obviously a non-standard sample type, but we will look at the data. And, if the data supports the use of a blood-based detection of virus, then we may be able to authorize that. Hopefully, that addressed both of your questions.

FFIM2601@gmail.com: Thank you.

Anike Freeman: Alright, that concludes the question and answer period. Thank you, everyone, for your participation. We greatly appreciate it. Today's presentation and transcript will be available at CDRH Learn in about a week. You can visit CDRH Learn at www.fda.gov/Training/CDRHLearn.

Note that we've updated the title of this section to make it easier to navigate. You'll now find the recordings in the subsection titled Coronavirus, COVID-19, Test Development and Validation Virtual Town Hall Series. For additional questions about today's presentation and topics, please send an email to CDRH-EUA-Templates@fda.hhs.gov.

As we continue to hold these virtual town halls, we appreciate your feedback about the program. Please complete a brief survey, which you may find at www.fda.gov/CDRHWebinar. Again, thanks for joining us today. And please join us next week on August 25 for the next webinar. This concludes today's town hall.