FDA Virtual Townhall

Moderator: Ivory Howard
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Coordinator: Welcome and thank you for standing by. Today's call is being recorded. If you have any objections, you may disconnect this time. All participants are in a listen-only until the question-and-answer session of today's conference. At that time, you may press star 1 on your phone to ask a question. I would now like to turn the call over to your host, Ivory Howard. You may begin.

Ivory Howard: Hello. This is Ivory Howard of CDRH's Office of Communication and Education. Welcome to the FDA's 58th webinar in a series of virtual Town Hall Meetings to answer technical questions about the development and validation of tests for SARS-CoV-2.

Today, Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health, and Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and Radiological Health both in CDRH, will provide a brief update.

Following the opening remarks, we will open the line for questions related to the development and validation of tests for SARS-CoV-2.

Remember that during the Town Hall, they're not able to respond to questions about specific submissions that might be under review.

Now I give you Dr. Timothy Stenzel.

Timothy Stenzel: Thank you and hello everyone. Welcome to another week of the Town Hall. We have some opening remarks and then we'll go into the received - the questions received prior to today's call and open the line.

We are still seeing a significant number of applications every week. I mean, and then as a monthly total for COVID EAUs, pre-EAUs, amendments, and supplements, we're seeing still around 160 to 200 applications a month. And this is keeping us very busy, especially since the surge in staff for COVID has largely returned to prior to the surge capacity and workload per reviewer.

So though the surge folks have gone back to regular MDUFA work, which does include COVID pre submissions, Q submissions, and full submissions for COVID assays. That does leave us back to a lower level of staffing for EUA.

And I just wanted sponsors and developers to know that. We're doing our best to keep up with the volume and largely we're clearing applications weekly at the same - approximately at the same rate that we're receiving them. So we should be cycling through on a pretty routine basis.

So but because we have fewer staff, our times for responses and everything may go up a little bit. This is unfortunate, we know. We're doing the best we can. We ask for your patience.

On the other hand, we've now authorized over 380 unique submissions and well over 500 supplements and amendments to date. So there is quite a significant number of tests available in the market. And we have seen testing go down across all categories in the U.S. and also the number of positive samples is way down. Let's remember that positive samples and percent positive rate going way down is great news for the country. I just want to put all that in context.

All right. And our priorities remain the same as most recently previously stated, diagnostic tests for point of care, in-home and home collection and high throughput central lab tests.

And I will turn it over to Toby. Thank you.

Toby Lowe: Thanks, Tim. Thanks, everyone for joining us today. I have one update. We - on Friday of last week, we issued a safety communication regarding a Class I recall for the Lepu Medical Technology's SARS-CoV-2 Antigen and Leccurate Antibody Tests. These were tests that had not been authorized, cleared, or approved by the FDA. And the company is recalling them under a Class I recall because they were distributed as unauthorized tests.

We are aware that they were distributed to pharmacies to be sold for at-home testing by consumers, as well as offered for sale directly to consumers. So that safety communication and Class I recall were posted on Friday of last week.

And then I can move into the handful of questions that we received ahead of time. The first one we have is related to comments that were made on a previous Town Hall recommending that for antigen and molecular test data subset should be provided in the EUA submission for vaccinated individuals enrolled in the clinical study.

And the questions being asked are for a point of care and over-the-counter EUA low cost for a lateral flow antigen test, what data should be collected from the enrolled vaccinated subjects to be provided in the data subset?

And if a vaccinated subject is confirmed positive or negative with both the candidate device and the EUA authorized highly sensitive RT-PCR comparator method in the clinical study, can the vaccinated subject be considered part of the confirmed positive or negative samples needed for the EUA submission?

So to address those, first, we would ask that the data be included in the clinical line data of additional columns and should include the date of vaccination, which vaccine was administered, and if it's a multi-dose vaccine the number of doses and the dates that were - that they were administered.

And then it may be acceptable to include all subjects together provided that they're not pooled retrospective and prospective specimens.

But we do want to see the performance stratified by nonvaccinated verse vaccinated individuals. And depending on the specific situation, we may request additional presentations of the data, such as one dose verse two doses. And we would also want to see asymptomatic and symptomatic stratified as well.

Our next question is about pooling of saliva specimens for previously authorized EUA assay. This company specifically has a PCR assay that has been authorized for use in either respiratory or saliva specimens. And they are looking to seek authorization to pool up to five saliva specimens.

So they're - let's see, they're asking about the template which states that a high sensitivity Real Time-PCR should be used to confirm that at least 25% of the saliva specimens pooled are low positives.

And also asking about whether they can use archived PCR positive saliva samples. So we did recently authorize the first saliva test for pooling. And that the Clarifi COVID-19 Test Kit by Quadrant Biosciences. And the publicly available decision summary for that EUA outlines the study details for saliva pooling approach. So we would recommend you take a look at that to get a better sense for what we are looking for.

And in that document, you will note that saliva samples were tested individually and in a pool to establish performance and no further comparator method testing is needed to establish a pooling claim for a previously

authorized EUA test for saliva.

And we also note that archive samples are acceptable to establish a pooling claim.

And then the last question that we have is from a company that is preparing a presubmission for a multiplex PCR gastrointestinal assay. And asking, based on the previous feedback about priorities, whether that would fall into one of the categories identified as priorities by FDA. So, again, those priorities are COVID-19 related, companion diagnostics, breakthrough designation requests, and a significant public health impact. And those relate to the presubmissions that we will be reviewing.

So we - as we've discussed previously on the Town Hall, those are the categories or types of IVD presubmissions that we intend to review at this time. Tests outside of those categories, we are not likely to have the resources to review right now. So we will be generally declining other IVD presubmission requests.

And this, based on the information provided in this question, it does not appear that this multiplex PCR gastrointestinal presubmission would fall into one of those categories. There are, however, other GI multiplex 510(k) cleared assays that can be referenced for the recommended analytical and clinical study designs.

And with that, unless Tim has anything additional to add on any of those questions, we can open the line up for the live Q&A.

Timothy Stenzel: I say we open it up. Take the live questions.

Toby Lowe: Great.

Coordinator: Thank you. We will now begin the question and answer session. If you would like to ask a question over the phone lines, please press star 1 from

your phone, unmute your line and speak your name clearly when prompted. Your name is required to introduce your question. If you would like to withdraw your question, press star 2. Again, to ask a question over the phone lines, please press star then 1. One moment as we wait for any questions. Our first question comes from (Annie Wright). (Annie), your line is open.

(Annie Wright): Hello. Thank you for taking my question. My question again is about the requirement for a mobile App after EUA approval for an OTC COVID-19 product. We just wanted to confirm because we, you know, we will be - we're in the process of developing a OTC product. And we realize that the - that there are requirements for mobile Apps for reporting.

So we're working - we're currently working with a mobile App contract manufacturer right now, supplier. And we just want to confirm that the main requirements that the FDA would like to see for the mobile App is basically the ability to report to health authorities only. Are there any other...

Timothy Stenzel: Yes.

(Annie Wright): ...requirements? We'd just like to confirm that.

Timothy Stenzel: Yes. So thanks for the question. I just want to clarify that this is not a requirement to make the initial authorization. We have authorized a number of OTC tests that didn't yet have a mobile App for reporting. The intent here is to assist in managing the public health crisis. And therefore, what we're asking is an App that can report positive and negative results to public health authorities, state, local, and national. So that's the intent.

And that and what we've been doing is arranging a post-market commitment for those developers who don't have a reporting feature at the time of original authorization.

(Annie Wright): Okay. Thank you so much.

Timothy Stenzel: You're welcome.

Coordinator: Our next question comes from (Ron Domingo). (Ron), your line is open.

(Ron Domingo): Hello. Thank you for taking my question. FDA has previously focused on testing using fresh samples for supporting antigen tests. However, with the growing complexity of obtaining fresh positive samples, the sponsor that we're working with would like to freeze samples collected during a post-EUA study, then use the frozen samples to support development of another assay for an EUA submission.

We're seeking FDA's feedback on this on an alternative approach to address the issues of obtaining sufficient positive samples at this stage of the pandemic.

Timothy Stenzel: We recommend that you check with us on your plans for banking for antigen tests, and to use frozen swabs, maybe direct swabs. And we're open to that pathway when enough positives can't be obtained in a prospective study quickly enough. We still want to see a prospective study, at least see the negatives and see the performance there and confirm performance and insights prospectively.

And hopefully, you'll see, well, not necessarily hopefully, but maybe you'll see some positives in that prospective study.

And then we're very open at this point to different methods of enriching those positives. And however, the details could be very specific to a given device. So we would ask you that you address these questions through, you know, a pre-EUA or if we have a pre-EUA to add that to the list of questions that you're asking the reviewer.

So a couple of things to consider is how do you source and select those positives? And, you know, is there introduction of any selection bias that

could impact evaluating actual test performance?

For example, if you were to use a very insensitive test to select those positives, you would be biasing your test population to higher positives. And we want to try to see the full spectrum of positivity from low amounts of virus to high amounts of virus, you know, in your - depending on your device, but for the claim period or time period wise.

And then also we have seen particularly for antigen tests where a pre-thaw cycle does increase the sensitivity of the assay. And so we would want to see some sort of freeze/thaw comparison study to a fresh sample.

And there's multiple ways to do this with a bank sample or other method so do check with - do propose something and check with the FDA Team.

And we would hope that there would be no bias introduced by the pre-thaw. That is, the test performance would be the same whether it's frozen prior or not. And then, you know, if there is a difference, assessing that difference and the impact on the study design. So those are some of my high-level thoughts. I don't know if Toby has anything else to add.

Toby Lowe: No, nothing to add.

(Ron Domingo): All right. Thank you for your detailed response, Tim and Toby.

Coordinator: Our next question comes from (Franco Calvert). (Franco), your line is open.

(Franco Calvert): Thank you for taking my call again today. My first question is related to the notice that came on Friday about the Lepu tests. And there was a mention that these tests were distributed through some pharmacy networks.

Is there any further detail as to what pharmacies or what distribution networks those tests were made available? Because we're talking about a .4 million antibody test and there are at least 205,000 antigen tests. And so that's one.

And the other one is a question related to the previous question. So we have been doing a lot of due diligence studies that would help us understand better the clinical performance of our test. And to do that we purchased, I believe, about 30 positive samples with CT values. And these are nasopharyngeal samples with various CT values. We have found a very positive concordance in general.

Now is there - given that the prevalence is low, as it has been pointed out many times, is there any way to use those samples as part of the official clinical validation or would we have to basically start from zero after submitting the protocol for the clinical validation to FDA?

Timothy Stenzel: You may be able to use that data in support of your submission. And I would suggest you come in with a pre-EUA to explain what you've done and ask that specific question. The things we would look at is how did you obtain those samples? Is there any bias? What was the comparator test used? Was it an acceptable comparator test? You know, is the range of positivity acceptable? And then was there any impact of the banking freeze/thaw on performance? You know, and was your protocols set ahead of time before you did this evaluation?

And there was another thought. Oh, and you haven't changed your device. And then the people who read the device are your intended use population?

So there's a lot of questions there. But bottom line, is it a sample type that you're seeking authorization for? Did, you know, the population that you're intending to be used for the test perform the test and interpret the test?

So those are some of the questions and there's a lot of questions there to address to find out if that study is acceptable for use in support of your application.

So again, I would lay that all out. I'd ask the team through a pre-EUA. If you've already submitted a pre-EUA, you can go back to the same reviewer and come in with some new questions.

Toby, anything to add?

Toby Lowe: Not on that aspect. I can respond to the first question about the safety communication for the Lepu test that went out last week. The information that is posted on our web site is all of the information that we have publicly available right now for the distribution of those tests.

(Franco Calvert): All right, thank you.

Coordinator: Our next question comes from (Howard Ernovitz). (Howard), your line is open.

(Howard Ernovitz): Hi there. Hello, everybody. I wanted to find out if, in fact, there's any guidance or guidelines that I can find that is regarding the next-generation sequencing or laboratory-developed tests, if you will, for long COVID, that is the post-COVID individuals. We're going to plan a study. We have some preliminary data that we may have a tool that could be diagnostic.

And I'm wondering in planning the study, is the number still going to be 30 symptomatic long COVID patients looking at 30 asymptomatic long COVID, or post-COVID at this point, and then perhaps 30 healthy? And thank you.

Timothy Stenzel: So just clarify the question, you said laboratory-developed test so this would be a test designed and developed and validated in a single lab or within a single healthcare system.

(Howard Ernovitz): Yes. Yes.

Timothy Stenzel: And the test you're going after is prediction of long COVID sequela. Is that the purpose of the test?

(Howard Ernovitz): Yes. The purpose of the test is to make a diagnosis that the gene sets that we are - or the first gene sets that we're looking at right now can tell the difference between people with active COVID infection and people that have recovered and are asymptomatic.

And so the genes involved in this make sense. They're all a very specific immunologic set of genes. So one single lab making a diagnosis that you, in fact, have a gene set that is more likely to be not recovered or COVID-related and then use it also as a modern test to see if, in fact, combinations of steroids, or the like, can be used in a liquid biopsy.

So the first application would be diagnosis and confirmation.

Timothy Stenzel: Diagnosis of long...

(Howard Ernovitz): Yes.

Timothy Stenzel: Okay, okay, so...

(Howard Ernovitz): Not recovered.

Timothy Stenzel: ...I'll address the technical question. I'm not sure of the LDT question. That'll be Toby. So and this is for anybody interested in this sort of test. And certainly, you know, this has been a topic. And but we haven't authorized such a test. And I'm not sure that we're ready to provide recommendations on the validation for those that are interested in developing such a test.

So at that point, I think I want to throw it over to Toby. Toby, if you 're ready to catch this one on LDTs, what our current stance on LDTs are.

Toby Lowe: Sure. I think that there's not a whole lot that we can say at this point about LDTs. That is still an issue that we're working through. But there - you know we do still have the guidance document out that discusses lab tests as well as

the HHS statement from last year.

Timothy Stenzel: Yes.

(Howard Ernovitz): Thank you.

Timothy Stenzel: So, you know, and the bottom line is the FDA has stated that they're not currently reviewing LDTs, and nothing's really changed on that. And I don't know that we can add anything else.

And then developers of this kind of technology that do want to, I'm going to say kit it, a traditional manufacturer, I would just say that if you're thinking about this, to come in through a pre-EUA and engage in a conversation with us. I'm sorry I couldn't be a little bit more encouraging of providing some information here at this time.

(Harold Ernovitz): Good. Thank you.

Coordinator: Our next question comes from (Ojune Sook). (Ojune), your line is open.

(Ojune Sook): Thank you. Yes. I just had a quick question that's similar to some of the questions that were asked before regarding the clinical evaluation of a molecular test for the EUA with the positivity rate and prevalence going down. We already have a study design and a plan to start for a prospective collection.

But our test specifically uses a direct swab as a sample type to be used for testing. So I was wondering if we wanted to go down the route of complementing the prospectively collected sample data with the bank samples or contrived samples if it's going to be acceptable to use contrived samples that have not been banked or diluted in the VTM or other matters that are usually done for frozen samples or bank samples.

And if we can just use those contrived samples near our limit of detection to

supplement or to complement our prospective data, or if we have to specifically find a banked sample with a known CT value that can be - that is somehow in a dry format. I don't know if that's possible. And use those for - to support the prospective samples collected for our study.

Timothy Stenzel: So I think what you're saying is what happens or maybe it's already happened. You've already done your study. And you're not getting a lot of low positives. And what do you do if you don't get enough low positives? And can you use bank samples in some way? Is that correct?

(Ojune Sook): I guess just to, yes, clarify. I'm just asking, you know, given the low number of positives and positivity rate, you know, we could be having trouble collecting all 30 prospectively collected positive samples.

So again, related to the questions asked earlier during a pre-Q&A session, we were also thinking of potentially supplementing the data, the prospective collection data with the banked or frozen samples.

But I was wondering if we can use the contrived samples as a set of supplementary data to support the prospective collected data if we cannot get all 30 positives within a reasonable timeframe. And if we do use the contrived samples, if we still have to do a comparator testing on the contrived samples.

Timothy Stenzel: Yes. I'm not sure what you mean by contrived, because you're talking about banked or frozen. So.

((Crosstalk))

(Ojune Sook): So yes. I guess just to again, sorry, clarify. Yes. There are two different types. So, I mean, one approach is to use the bank samples. But another approach I was thinking of doing this was just to use a contrived sample with a - the viral - virus particle spiked into the negative swab.

Again given our test is a dry swab, I was thinking making a contrived sample

at a very low LOD or close to our LOD would be more straightforward than finding the bank samples that would be, I guess, amenable to be used with our testing protocol. So, yes. I'm not sure if I'm making any sense here.

Timothy Stenzel: Well, I just want to be clear. So we're not currently entertaining contrived samples. As I mentioned at the top of the hour or at the top of the call, we've authorized now over 380 EUA authorized tests. And going back to contrived samples would be obviously something that's quite challenging, especially in the face of testing demand and testing utilization going down so.

(Ojune Sook): Okay.

Timothy Stenzel: We're of the mind that there are more than 30 banked samples out there. That we're open to using banked samples if you've attempted a prospective collection and been unable to achieve the recommended number of positives. And then if you're going to move to banked to - we recommend that you check with our Review Team to make sure that that process of going to banked is done in the least biased way and the proper validation is done around the use of banked and frozen samples.

(Ojune Sook): Okay. Thank you.

Coordinator: Our next question comes from (Roseanne Chan). (Roseanne), your line is open.

(Roseanne Chan): Hello. Hi. Thank you. Yes. I have a general question. We haven't heard about high sensitivity COVID RT-PCR Tests. Is this list of tests on the FDA web site or what is the definition of a high sensitivity COVID RT-PCR Test?

Timothy Stenzel: So we do recommend that you do check in with the Review Team during your pre-EUA or ask a very specific question in your email box for your test whether or not a particular central lab molecular test is sufficiently high sensitivity.

We're looking at those tests that are towards the high end of sensitivity and have a separate extraction/concentrating step before going into a PCR. And an RT-PCR assay is important because we're looking at the CT values in that comparator to assess how - whether the range of viral loads in your study set so that we can evaluate performance across the dynamic range. Not dynamic range but among the, you know, expected level of virus in a usual population.

(Rosanne Chan): All right, thank you.

Coordinator: Our next question comes from (Ron Domingo). (Ron), your line is open.

(Ron Domingo): Hi. Thanks for taking my question again. This is related to some previous comments and questions. We talked about the dropping positivity rate and rising vaccine rate. And sponsors think that it's going to be difficult to achieve the sample size required by FDA during the post-authorization study in a timely manner.

So what other options are available to the manufacturers for achieving post-EUA numbers? Would the agency consider reducing the sample size or restrict studies to a fixed period of time or would you also consider data collected outside of the U.S.?

Thank you.

Timothy Stenzel: And so this is conversion of an EUA authorized assay to a full authorization assay.

(Ron Domingo): Yes.

Timothy Stenzel: So I have been encouraging recently that you come in with a presubmission. It's not a pre-EUA. It's a pre, but it's actual usual qsub presbmission. We are accepting them for COVID. And we will address those questions.

And, you know, because of the current situation we'll be as flexible as possible on that situation. And we are looking to all possibilities using actual patient samples from banked to samples collected internationally and even the testing performed internationally if that's the best way to validate the test.

But again, come in through the presubmission and ask those specific questions to make sure that depending on the characteristics and the design of your test and where you're able - where you're intending that test to be used so that we give the most specific feedback we can on your particular device.

But yes, now's the time to really convert assays and something I probably should have mentioned at the beginning of the call as well. Just come in with those presubs and qsubs now and be working on your conversion if you want to stay in the market past when the declaration might be ended at some point.

(Ron Domingo): Okay. And Tim, if it wasn't a conversion submission, would your recommendation still be the same?

Timothy Stenzel: So you come in through - if it's not been EUA authorized yet, then come in through a pre-EUA and ask about alternate ways of getting a positive. But again, we want to see a prospective study as we would recommend. And it's only when you've demonstrated that the inability to collect all the positives that we would look for alternative methods to accumulate more positives in your study.

(Ron Domingo): Okay, thank you.

Coordinator: Our next question comes from (Ashwood Doman). (Ashwood), your line is open.

(Ashwood Doman): Thank you very much. My question relates to decisions made by the FDA late last year, around October, November. I don't want to make this about any particular number of companies, but some companies received de-prioritization notices, including those that had, you know, rapid antigen tests

with potential for at-home applications. I was wondering if these notices would require these companies to reapply or have they - have their EUAs been automatically put back into the application's line?

Thank you.

Timothy Stenzel: So in general, it depends on the reasons for the de-prioritization. But if it was, you know, a home test and point of care test that's still a high priority, so it would not have been de-prioritized for that reason.

So sponsors would've gotten some sort of information from the FDA on why we declined to review or declined the issue. Those are the two main de-prioritization reasons.

And if the - a developer is able to address those concerns and wants to come in with a subsequent submission, they are free to do so. The FDA's concerns, though, would need to be addressed. Otherwise, the result may be the same.

(Ashwood Doman): Okay, thank you.

Coordinator: And...

Toby Lowe: And I think to clarify a little bit about that question, if the test, you know, sort of otherwise appeared to meet the priorities, I think you mentioned a rapid antigen test with a potential for at-home use, they may have been de-prioritized not because they didn't meet priorities, but because there was something lacking about the submission.

And so I think that's what Tim was really getting at with, you know, needing to look at the specific reasons that were given to the company so that the company can address those issues prior to resubmitting.

So, for example, if it has potential for at-home use but was not validated for at-home use then that would be a potential reason why a test may have gotten

one of those letters. And we would want to see that validation completed prior to resubmission.

Timothy Stenzel: Or there could be some kind of performance issue or...

Toby Lowe: Right.

Timothy Stenzel: Or, you know, inadequacy of the studies or design or something. So, again, that response from the FDA is specific and tailored to each developer so that the developer can decide what to do, you know, address those in an appropriate manner and come back in or not. But we endeavor to be very clear and transparent in our feedback to each of the sponsors.

Coordinator: As a reminder to ask a question over the phone lines, please press star then one. Our next question comes from (Juanita). Your line is now open.

(Juanita): yes.

Timothy Stenzel: Hello. Cannot hear you.

(Juanita): Hi.

Coordinator: Your line is open.

(Juanita): Hello. Can you hear me?

Timothy Stenzel: Yes, we can hear you.

(Juanita): Oh yes. Okay, thank you. Yes. I think my question has been answered. Thank you so much.

Timothy Stenzel: You're welcome.

(Juanita): Okay, all right, okay. Bye.

Coordinator: We have no additional questions in queue at this time.

Timothy Stenzel: Let's hold for one or two minutes. And if there are no questions, we can end the call early. And again, thank you for everybody calling in and for asking these questions. Hope that we have been transparent and have been able to clarify and provide specific guidance or and recommendation.

Coordinator: We have another question in queue. Our next question comes from (Elizabeth Brinley). (Elizabeth), your line is open.

(Elizabeth Brinley): Hello. I just wanted to clarify something that I thought I heard on the call earlier. Did I hear you correctly when or when I heard that you thought that maybe the EUA would be terminated next month?

Timothy Stenzel: No. I'm not sure where that came from. Toby, do you know where that might've come from?

(Elizabeth Brinley): Okay. I must've heard something. Well...

Toby Lowe: No, not all.

Timothy Stenzel: Do you know?

Toby Lowe: I don't think that we would - I don't think we said anything.

(Elizabeth Brinley): Okay.

Toby Lowe: About that.

Timothy Stenzel: So.

(Elizabeth Brinley): Okay. Thank you.

Timothy Stenzel: We don't think...

Toby Lowe: No.

Timothy Stenzel: ...that the current emergency declaration will end any time soon, which means that the EUA pathway will remain open and EUA authorized tests will remain available. Should a time come when it comes time for conversion to full authorization, the FDA will provide guidance and a pathway, you know, and allow, you know, reasonable time to come in with a full submission all the while allowing the EUA authorized tests to remain on the market so that we meet our nation's testing needs.

We're - as far as I know, we're nowhere near that. And the guidance, our draft guidance hasn't been made public yet. And as soon as we can, that'll be made public so that all developers understand, you know, what they're looking at in a post-emergency declaration situation.

But, you know, we're not - in my estimation, we're not anywhere near that. That's going to be a long time off.

(Elizabeth Brinley): Okay. Thank you for the clarification on that. One other question, are you still recommending that if an EUA modification and/or submission was made weeks ago that we follow up with an email and include you and Toby on the email?

Timothy Stenzel: Occasionally, we do give that advice. And I'm sorry. What was the topic again?

(Elizabeth Brinley): You know we submitted a modification to an EUA that was submitted last year and then an additional EUA to couple with that for home collection several weeks ago. What would be the best way to follow up for that?

Timothy Stenzel: If you've been assigned a reviewer or a contact, you should've been except maybe the most recent submission if it's within two weeks. But you should

have a contact and you can reach back out to that contact. If you're not getting any...

(Elizabeth Brinley): We do not have a reviewer. Okay.

Timothy Stenzel: You have a contact. You have a name...

(Elizabeth Brinley): Yes.

Timothy Stenzel: ...of an FDA person.

(Elizabeth Brinley): No. Well, I have somebody that we used last year, but not somebody that was assigned this year. No.

Timothy Stenzel: Yes. And so I would go back to the templates email inbox and try to seek clarification. And if they cannot clarify for you that the status, then ask for your email to be forwarded to Toby and me.

(Elizabeth Brinley): Okay, thank you.

Coordinator: Our next question comes from (Dana Hummel). (Dana), your line is open.

(Dana Hummel): Thank you for taking my question. We would like to get the FDA's feedback on our proposed clinical study protocol. However, we have not submitted a pre-EUA yet. Would it be okay to request feedback on our protocol before we submit a pre-EUA?

Timothy Stenzel: That would be the purpose of the pre-EUA is to put the protocol in there and any other details about your assay for us to evaluate your protocols. Anything that's clear from our template doesn't need to be asked. And it's only things that are outside of our recommendations. And if you want to confirm the comparator you're using is a suitable comparator.

(Dana Hummel): Okay. We were just still compiling all the information for the pre-EUA. But

we wanted to get started on the clinical study. So that's why I thought maybe we could just get your feedback on the clinical study protocol before we put together the entire pre-EUA.

Timothy Stenzel: It's probably more efficient for you to get everything together.

(Dana Hummel): Okay.

Timothy Stenzel: And then our team has everything to review. You're going to want to have that feedback before you start and so looking at just one part of a potential pre-EUA, you know, isn't necessarily the most efficient way to go about this.

(Dana Hummel): All right, perfect. Thank you.

Coordinator: Our next question comes from (Franco). (Franco), your line is open.

(Franco Calvert): Thank you for giving me the opportunity to ask a couple of more questions since there's a light audience today. The first one is regarding a sensitive control step that we have been doing at our own discretion, really because we have been generating the sensitivity of the antigen test.

So since the Abbott BinaxNOW, the Quidel QuickVue, and a couple of others can actually be bought now directly from pharmacies, we actually got our hands on a couple of Abbott BinaxNOW and, I believe, the care test from Axis Bio. And we used the most positive control with the specimens that we purchased, which were in CDC VTM.

And I wanted to also provide a little additional detail about how we obtained those. So basically, and this would address the issue of the bias, perhaps.

So basically, we hired a lab that has been doing a lot of testing through the pandemic. And they use a high sensitivity PCR test with an extraction step. So we knew that from the get-go. So basically what we did for those 30 samples was we said, hey when you get a positive, let us know. We like to

test that person to see, you know, how our test performs. And that's, in effect, how we ended up getting those 30 specimens.

So would that be a biased way? So that's what is related to my first comments regarding - are you aware...

Timothy Stenzel: Yes. So...

(Franco Calvert): ...about the - sorry. May I continue?

Timothy Stenzel: Yes. But hold on a second, though, because this is getting very specific advice for your specific submission.

(Franco Calvert): Okay.

Timothy Stenzel: And it's not it's not something that we typically do on the call.

(Franco Calvert): I apologize.

Timothy Stenzel: So the best way, though, to get - because in all likelihood, I'd need more detail than you're giving me right now to address bias. And so the usual way for us to do this is actually see the study protocol.

(Franco Calvert): Okay.

Timothy Stenzel: How are you acquiring samples in the context of your specific assay and use case?

So those are all important to assess, you know, the acceptability of what you propose and takes a little bit more time to assess than we can on this call.

(Franco Calvert): Sure. I apologize. Thank you.

Timothy Stenzel: No reason to apologize.

Coordinator: Our next question comes from (Shari Kosick). Your line is open.

(Shari Kosick): Hey, Tim and Toby, can you hear me?

Timothy Stenzel: Yes.

(Shari Kosick): Oh, hey, thank you very much for taking my call. You guys are wonderful and the D&D Group needs to win some kind of an award for the EUA nightmare that they're going through.

But I have a question about pre-EUAs. We submitted a pre-EUA template about six months ago and got a response about two weeks ago. If you're planning a clinical study for a EUA for SARS-CoV-2 EUA, and if we submit a clinical study to get your opinion on using bank samples, what is the timeline for response? Do you have a clue of, you know, is it like 30 days, 60 days, 90 days or whenever it comes, it comes?

And the reason I'm asking...

Timothy Stenzel: We're on a...

(Shari Kosick): ...it is because we're on - sorry. Go ahead.

Timothy Stenzel: No, no, no. I cut you off. Go ahead.

(Shari Kosick): No. I was just going to say the reason I asked is because we have to get the clinical sites up and running and there's a lot of planning that needs to go into place. And it would be useful to sort of understand what kind of timelines we're seeing for pre-EUAs when specifically questions regarding how to do the clinical study or is archive samples okay?

Timothy Stenzel: Yes. So the team is working on how best to use archive samples right now. So hopefully on a subsequent call, I can provide more global harmonized

information. For now, yes, and, you know, if this is a priority submission. If they don't get back to you with an idea within two to three weeks, you know, ask them to - ask the templates email box, with a copy to D&D, and we'll work on getting you faster response. As I said at the beginning...

(Shari Kosick): Thank you very much.

Timothy Stenzel: ...of the call, we remain very busy and we're back down to basically non-surge staffing right now.

(Shari Kosick): Yes. And that's the reason why I think really D&D is doing a wonderful job considering the fact that you guys are dealing with so much. So I mean, I really appreciate the reviewers for their time and your time, too.

But, you know, even we are strapped on our side too so you - I know you understand that. Thank you.

Timothy Stenzel: Yes. We've received over 5500 applications in a year, including COVID and non-COVID applications with 300, well actually, yes, for 300 staff. So it's a large volume. Thanks.

(Shari Kosick): It's an amazing thing. Thank you.

Coordinator: We have no additional questions in queue at this time.

Timothy Stenzel: I think we can go ahead and close the call Operator. Thank you.

Coordinator: Thank you for your participation in today's conference. You may disconnect at this time.

END