FDA Virtual Town Hall Series – Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests

Moderator: Irene Aihie
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Coordinator: Good afternoon and thank you for standing by. For the duration of today's conference, all participants' lines are in a listen-only mode until the question-and-answer session. At that time if you would like to ask a question, press star 1. Today's call is being recorded. If you have any objections, you may disconnect at this time. It is my pleasure to introduce Ms. Irene Aihie. Thank you, ma'am. You may begin.

Irene Aihie: Thank you. Hello. I'm Irene Aihie at CDRH's Office of Communication and Education. Welcome to the FDA's 39th in a series of virtual town hall meetings to help answer technical questions about the development and validation of tests for SARS CoV-2 during the public health emergency.

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

Following opening remarks, we will open the lines for your questions related to the development and validation of tests for SARS-CoV-2. Please remember that during the town hall, we will not be able to respond to questions about specific submissions that might be under review.

Before I turn the call over to Timothy, I would like to let the participants know that we will not be holding a town hall next Wednesday, January 20. We will resume on Wednesday, January 27. Now I give you Timothy.

Dr. Stenzel: Thank you, Irene, and welcome, everyone, to another town hall today. I have a few topics to cover before we get into the questions. We had two safety communications last week. I just wanted to go over them at least at a high level.

The first one had to do with the Curative molecular EUA test. We are recommending no off label use. Again, no off label use. The test, nasal swab and oral fluid, are to be only used with patients who are symptomatic and in the first 14 days of symptoms.

We are warning against false results if these procedures are not followed. In addition, if an oral swab test is a negative, it should be confirmed with another test.

You know, for those who are concerned with results they may have received, if those results are more than 14 days old, there's really nothing that we recommend doing. However if the results from Curative have been received within the last 14 days, do look at the entire clinical picture and if warranted test with another test.

The second communication which happened late last week had to do with mutation. As we know, variants of SARS have been a hot topic for a little bit now.

From the very beginning of the pandemic, the FDA has been asking all developers of tests to do an in silico analysis to make sure that their tests are inclusive of all known mutations.

That mutation database has grown over time and continues to grow. Mid-summer, the FDA began a more active surveillance of those tests that had been EUA authorized.

We know all of the primer and probe sequences for molecular tests and we also have access to the GISAID database. And so we do an analysis on a regular basis of the GISAID database.

We search for mutations that exist in a prevalence. Right now we're about 5%. And the reason we chose 5% is that if the test has a decreased sensitivity of 5% or more and in particular a molecular test that may be near 100% and falls 5% or more, it falls below 95% sensitivity, then that's something that we definitely want to look into.

No matter what, when we identify a test that may be impacted by a variant of importance at that 5% level or in the case of the South African variant and the UK variant, we have or are in the process of reaching out to all test developers of the EUA authorized test to have them, in conjunction with us, do a review of the potential impact of those mutations.

So prior to our safety communication, we had done a search for the UK variant and the South African variant. We did mention three tests in the safety communication.

Those tests were either impacted by the UK variant or another variant. The other variant was a GGG to an AAC at position 28881. And so there were two tests that were potentially impacted by the UK variant, particularly the Δ69/70 deletion.

The S gene target or one of the S gene targets in both assays were impacted to the point where we don't think that it would be positive on the UK variant. However both assays were multitarget assays. The Thermo Fisher TaqPath had three targets and the Linea assay has two targets.

Because they are multitargeted and the other targets were functioning in the UK variant, we don't expect that there would be a decrease in sensitivity. And therefore the prime reason for us to review these two tests is they are the only tests that we know that were EUA authorized that would - excuse me? That would potentially identify the UK variant.

Of course, not all variants that carry the Δ69/70 deletion are the UK variant, in fact only a small subset for right now. So sequence confirmation is recommended.

So local labs may have their own sequencing or state and local labs may - other labs may have some capability. And, of course, the CDC is doing a sequencing analysis and labs can reach out to the CDC for any guidance.

We have also authorized a sequencing base EUA that covers the entire viral genome and that is the Illumina SARS test. And so that is an opportunity for labs to confirm whether or not they have a UK variant.

We would ask that where labs are capable of doing this that the labs do this that they submit as many sequences that they generate as they can into databases so that the FDA can continue to monitor the databases for variants.

And this would be not just be the UK variant but all sequences. It's important that we get as many sequences as we can in the database and be able to understand a little better perhaps the true prevalence of what some of these variants are.

The other tests that were mentioned in the safety communication was the Mesa Biotech Accula, I believe, test. They are a single target test and they were potentially impacted by the GGG to AAC mutation.

They have updated their labeling to show the potential impact of this mutation. However at this time the impact seems relatively minor and we don't expect that any significant drop in clinical sensitivity will be seen in this assay.

This is a point of care molecular assay and I do believe that it's still useful to be used. And we just want users to be aware that in all cases, because these kind of false negatives from these variants can happen with any test and false negatives can happen with any test, so the patient context and all other clinical information for any negative should - of course, it should always be entertained that any given single test result might be falsely negative.

We will continue to surveil the variants that pass our threshold for routine reaching out to sponsors. But we'll also continue to surveil new variants that may be of important public interest.

When we find something that deserves to be shared with the entire community, we will update our safety comm to do so. And then, of course, it goes without saying that single target assays do have a slight disadvantage in the situation where we're seeing multiple variants relative to multiple targeted assays.

So I think we've gotten to the point in this pandemic with enough variants and sequences that developers should consider this carefully. We would also ask developers to continue to monitor the situation themselves and be very proactive and if they spot an issue to please contact the FDA.

All right. The last thing I wanted to mention was that our surge of putting additional resources on EUA reviews is making significant progress. We are still receiving a high volume of new submissions on the order of about 40 EUA submissions a month - I mean a week so about 160 a month.

That is a high volume and yet we're focused on a net decrease in open applications so that we can, you know, go through all of the open EUAs and also as a very robust and efficient process for the new EUAs.

So it is making now a significant impact on the net closure and that's evidenced by more and more authorizations as you've seen. But we are making all sorts of decisions at a faster clip now.

So with that, I think we can open it up to questions. Thank you.

Coordinator: Thank you. If you would like to ask a question, please ensure your phone is not muted, press star 1. And when prompted, clearly record your first and last name so I may introduce you.

Again, to ask a question, press star 1. Our first question is from Shannon Clark. You may go ahead.

Shannon Clark: Hi, Dr. Stenzel. This is Shannon Clark with UserWise Consulting. I can attest to those swift responses. Thank you FDA for your focus and speedy replies.

So my question and - can you hear me? I just want to make sure I'm not talking to myself.

Dr. Stenzel: Yes. Yes, Shannon.

Shannon Clark: Thank you. So our focus at UserWise is usability studies in human factors so my question is around that. And my question is about post-authorization software changes for tests for home use so Imugen molecular antibody test.

I imagine one of these employs a phone application. It has authorization. If a change is made to that phone application, which was used in the human usability testing, so say a change was made to text on the results screen to better align with FDA recommendations, which are everchanging. And then maybe there's another example where it allows you to skip an automatic timer that was previously there to accommodate the use scenario where they start the timer late.

So if a change were made of these sort of levels of change, would we need to submit a notice to the FDA and/or would we need to submit an authorization or can we internally justify it and proceed ahead?

Dr. Stenzel: That's an important question that I'm not sure that I have the best possible answer right now. Certainly we love to see improvements and increased safety with software.

It never hurts to communicate with your reviewer for the - original reviewer for the application to see if they have any concerns about that.

Obviously if there's any potential for degradation of performance, we would want to absolutely review that.

Toby, do you have any thoughts on this? I'm not sure where that leads.

Toby Lowe: Yes.

Dr. Stenzel: The pandemic obviously has continued to go on much longer than we anticipated. And we are seeing a whole host of questions that only crop up when a pandemic and a lot of development continues.

So, Toby, any thoughts?

Toby Lowe: Can you hear me?

Shannon Clark: Yes.

Dr. Stenzel: Yes.

Toby Lowe: Okay. Yes, so I think this is a great opportunity to have these discussions about potential software changes with your reviewer prior to your initial authorization.

There are situations where we might be able to build into the authorization what we often refer to as change protocols so that we would work with you ahead of time to work through what validation you would need to do for those changes and what metrics you would need to hit in order to not come in post-market with those software changes or post-authorization. But there may be other situations where we would expect to see a supplemental EUA request to update depending on what the changes are.

So it's a really good idea ahead of your initial authorization to talk through what source of software changes you would anticipate so that you can come to an agreement with your lead reviewer on the best approach for each of those types of changes.

Shannon Clark: Thank you. And over the past decade the FDA has been amenable to sort of smaller scale usability testing so, for example, skipping the timer. Many times in our submissions historically over the past 10 years, we can submit, like, a smaller scale usability study to justify that no undue harm could occur.

Is that sort of your line of thinking or do you think that due to the strict guidelines of authorization, we're at risk of having to repeat 100 person usability studies?

Dr. Stenzel: I would like to avoid a full repeat. So I think a scaled down version is acceptable in the specific situations with the specific changes would be ideal. And, you know, I would hope to be able to do that in all cases.

If there's major changes that might impact performance that might be different. But in general these kind of changes should be amenable to smaller scale user studies.

Shannon Clark: Thank you so much.

Coordinator: And our next question is from (Jackie Chan). You may go ahead.

(Jackie Chan): Hi. Good morning. I have a question about the neutralizing assay. And we are interested in - and this is a question about the validation requirement on the semi-quantitative neutralizing assay.

We would like to show concordance of our test against the PRNT assay. And my question is will a three concentration breakdown of the whole assay range be sufficient?

And also what is the current expectation on the percent agreement and the plus or minus agreement? Is it still 60% and 80%?

Dr. Stenzel: So we have not - have we released the neutralizing antibody template, Toby? I don't think so.

Toby Lowe: No, not yet.

Dr. Stenzel: But for the time being, you can inquire either of your reviewer or at the template's email address with what our current thinking is on neutralization assays.

The neutralization assays do not have to be semi-quantitative but they can be. And they may be more useful if they are. I think you mentioned three buckets. That's likely to be acceptable, but I would check with our review staff and our current thinking there.

(Jackie Chan): Thank you.

Dr. Stenzel: And the PRNT is the gold standard so that's good. We will want to look at the particular one that you're using as a comparator and make sure that we understand the validation of that assay as well.

(Jackie Chan): Okay. Thank you.

Coordinator: Our next question is from (Jenna McCarthy). You may go ahead.

(Jenna McCarthy): Hi. Thanks for taking my question. So FDA has said that it's prioritizing EUAs for certain test kits, including those that could be performed at the point of care or using at-home collection or testing.

We're aware that FDA is declining to review serology test EUAs that can only be performed in moderate or high complexity lab environments. But I wanted to know if FDA would review an EUA for a serology test that does meet its stated priority so, for example, one intended for point of care or at home use or is FDA signaling a broader de-prioritization of all qualitative serology tests? Thank you.

Dr. Stenzel: We've only authorized a small number of point of care serology tests. It has been a priority and continues to be a priority to authorize point of care serology tests and at-home, either prescription or OTC, the qualitative lateral flow test. So it remains a priority.

However we have authorized a number of moderate to high complexity lateral flow tests. We've also authorized a number of really high throughput central lab tests.

And so because there's so many high throughput central lab tests authorized, the need for a moderate complex or high complex test given our workload has diminished.

And so we are eager to review point of care tests of all sorts and especially those that come in with, you know, all the good studies that have already been performed so that we can evaluate the tests.

We continue to get point of care submissions that don't have the point of care validations done. So that's obviously problematic. We won't make a test submission a high priority unless we have, you know, all the point of care validations done and submitted with the package.

We are looking more closely at submissions. And if they are missing key elements, especially that are in our templates for the various applications, we are doing an RTA, which is Refuse To Accept. Some developers may be starting to see that.

We do a quick review. And so that communication should happen within about a 10 day window from receipt. This is really being applied to every application now.

It's very inefficient for our staff to get an application that's incomplete. And so we have screeners that are looking at these applications and making sure that they're complete.

If they're not complete, we are giving this really quick feedback so that developers can complete the studies and come in with a full package that we can spend time reviewing.

(Jenna McCarthy): Great. Thank you.

Coordinator: And our next question is from Steven Gonzalez with Ropes & Gray. You may go ahead.

Steven Gonzalez: Hi. My question has been answered. Thank you.

Coordinator: And our next question is from (Franco Calberone). Your line is open.

(Franco Calberone): Thank you, Dr. Stenzel. I think you just partially answered at least part of my question in terms of the completion of the submission.

I was wondering if the antigen review teams have become aware that developers that have their tests made outside the U.S. are having a difficult time finding the analytical validation resources in the U.S.

So it has been our experience that there are very few options available. Those that are available, you know, are picked up, you know, for months, three months, four months, you know, into the future.

And I was wondering if FDA would consider, let's say that we are able to complete the human usability and the clinical validation for the assay for home use.

Would FDA consider maybe allowing - maybe issuing a pre-EUA that - we can commercialize it but then, you know, give us some time to complete the analytical as to - you know, give us time for the resources, you know, the BSL3s and so on to get to us, you know, to solve our problem. That's one part of the question.

The other part, could you speak to FDA's presence of the reporting portion of let's say an at-home antigen test> If we were to not go with that in, you know, the first place, would FDA, you know, sideline an application like that? Those are my questions. Thank you.

Dr. Stenzel: Yes. Let me take the last question first. So we do ask what the reporting plans are for point of care and at-home tests. However having a plan in place is not a requirement for an authorization.

However we are asking developers who haven't come with a reporting plan for authorization that in the post-authorization period that they work to develop a reporting method. That could be an app. That could be a Web site.

HHS had a design-a-thon that has progressed and the winners have been selected.

And so our team can put you in touch with some of these software developers so that even in your development phase so that you can begin to work with them. And if not prior to authorization then hopefully shortly after authorization, those reporting opportunities can be put into place.

So the short answer is we would not hold up an authorization if there's not a reporting opportunity at the time we can make an authorization decision. But we certainly want to see developers, post-market at least, develop an opportunity.

And we're doing our part with the design-a-thon. And there are a growing number of apps that can be used on the Web site.

The first question had to do with analytical studies. They are very important. And we do need to see those studies. And we can sometimes offer flexibility because some things are just not available like SARS and MERS. And at least in one of them, they're difficult to culture coronaviruses. But those are very important for us to make a decision.

The user studies and the clinical studies for point of care in our homes, need to have sufficient U.S. testing because the point of care environment in the U.S. is frequently different.

We've seen point of care studies done outside the U.S. but they were really done in a central lab with trained laboratorians. And that's not the intended use population for waived tests in the United States.

And then, of course, the US users and languages are important here as well. So we want to see data from the US.

What's in our templates are recommendations. If there is an appropriate alternative, we can discuss that with you. It's best done prior to starting your studies so that you don't go into a study and then find out that it's not sufficient. So that can be done through the pre-EUA process to check study design.

The surge, and our desire to turnaround applications and more quickly and clear up some of the older open applications, we also have an effort to close pre-EUAs as soon as possible. And so we're hoping that as this surge in workforce continues that all developers see better turnaround times on pre-EUAs as well as the EUAs.

(Franco Calberone): Okay. May I maybe reframe the question a little bit, the first part of the question? So I think you mentioned FDA would be flexible to the analytical part. What does that mean exactly?

So the issue is really timing. So we finally have been able to identify the solution provider. But, you know, they're not going to get to us, you know, probably until three months from today so.

But on the other hand, you know, we do feel fairly confident about the other part, the clinical part, the usability following exactly the guidelines that you just mentioned. We intend to do everything in the US. So could you speak a little to what that flexibility may mean on the analytical side? I'm just thinking the FDA does want to see that.

Dr. Stenzel: Well, yes, we would like to see complete validations. We have on occasion authorized tests that have not completed every analytical study and sometimes not every recommended clinical study and those all go into post-approval condition of authorization with the timeline. So it depends.

And that's where it's probably very dependent on the particular application and what can be completed in a timely way and what can't. And it would be difficult for me to say, well, if you do this, this and this then you're okay on this call. I just...

(Franco Calberone): Okay. Got it. Thank you.

Dr. Stenzel: Okay. So that's to be worked out with your individual reviewer. We want to see, obviously, enough data premarket so that we have confidence that the tests will be able to stay on the market after the post-market studies are done.

(Franco Calberone): Right. Okay. Thank you.

Coordinator: Our next question is from (Annabelle Tsai). You may go ahead.

(Annabelle Tsai): Hi. Thanks, again, for doing these town hall series. They've been very helpful. My question is in regard to clinical evaluation for serological assays.

I'm curious if we enroll subjects who are symptomatic or who were symptomatic, who were PCR negative but have been vaccinated and therefore test antibody positive, will they still be considered false positives on our serological assay?

Dr. Stenzel: Someone who has been vaccinated and turns positive, you know, within a couple of weeks of a vaccination, it wouldn't be surprising that they would turn positive by a serological assay.

(Annabelle Tsai): Exactly.

Dr. Stenzel: So although I don't think we know enough about the serological response in a patient to be able to blanket say what we would do with somebody who is post-vaccine.

And, you know, that's something that's best put into inclusion and exclusion criteria for your clinical study. So for all clinical studies, we do want to see clinical study designs and we do want to look at your inclusion and exclusion criteria and make sure that things are done appropriately.

So if you want to exclude people who got vaccinated and are PCR negative, that's probably at this point an acceptable exclusion criteria.

In the future we may understand a vaccination better and that might be something we want to incorporate into clinical study designs as we go forward.

And if someone wants to include a subset of people who are vaccinated at this point, I think, you know, we can look at that.

Now the antibody response to vaccines, it's a further leap to say that because they generated antibodies then they have immune status or a given immune status.

I think we're too early on in the science here to say anything definitively about any immune status. But we're open to study designs that would address that question. They are likely to be large studies though and may be prohibitive because of their size.

(Annabelle Tsai): Okay. Thank you. We've thought about excluding but we were just worried that in time that might make the study very difficult to enroll enough subjects as more and more people get vaccinated. But I appreciate your thoughts and that's very, very helpful. Thank you.

Dr. Stenzel: Well, unfortunately, the last number I heard recently within a day was 9 million have been vaccinated. So we still have, you know, 321 million plus so.

(Annabelle Tsai): Right.

Dr. Stenzel: Okay.

(Annabelle Tsai): Okay. Thank you.

Coordinator: Our next question is from (Brian Jones). Sir, you may go ahead.

(Brian Jones): Yes. Last week you mentioned that there would be separate categories for single target SARS tests versus panel tests when applying for a de novo or 510(k). And I understand the FDA is drafting a guidance document for this.

My question is if a single target SARS test is built on the same technology as a panel test, but the panel test de novo is granted first, then can the single target test be submitted as a 510(k) using the multi-target test as predicate?

Dr. Stenzel: Well that's an interesting thought. And, you know, these special controls that are written with de novo applications and become part of the regulations have certain limitations.

So some of this is, you know, how can we adequately carve these things out? So our current thinking is that for a molecular or an antigen panel versus a single target assay that those would still be different on de novos.

So we're really talking primarily just probably two first de novos for molecular testing and two first de novos for antigen tests and then after those four de novos then everybody else is 510(k).

I would also just reiterate that we're not in a rush to ask developers to complete a conversion. Because of the large volume of EUA submissions that I mentioned, you know, at the top of this call, we're getting 160 new applications roughly a month still at this time period.

Our focus in the COVID sphere is to get as many EUA authorizations out as possible and to have a timely review of all EUA submissions. And, you know,

I think at the point where those submissions start to trickle off perhaps at some point, that's going to be a more ideal time to encourage conversions.

Because right now our focus for the COVID application is on EUAs. And we would probably put on hold most, if not all, conversion submissions. It doesn't mean we won't get to them. It's just that the priority right now is EUA.

So I'm not encouraging at this time full submissions until we get, you know, our turnaround times on EUA submission and get this down into an acceptable territory because we have the right staffing to manage the workload.

We are drafting a guidance. It probably will not be - it's going to be center-wide for all devices that are COVID related. And so we will not probably dive down in sufficient detail and probably technology on what the specific criteria are that we're going to ask for full submission rather that will be communicated in other ways.

I have asked our team to be able to provide the kind of information that we've provided in templates for SARS so that we can streamline Q-Sub or pre-submissions or full submissions. And that will be an efficient approach to handling those important Q-sub and pre-sub submissions on conversions.

The guidance, rather, is meant to lay out the framework and the timelines for conversions having to do with converting to de novos and then some 510(k)s and also on quality systems.

We waive most of the quality system requirements for EUA applications. But we will phase those out through this transition process after our first draft guidance obviously and then a final guidance.

Once the final guidance is issued then it will explain, you know, the timeline and those will most obviously be related to any point that the emergency comes to an end, which I don't foresee happening for a very long while.

So hopefully I've explained enough detail for you and others who are curious about this topic.

(Brian Jones): Thank you.

Coordinator: Our next question is from (Susan Sheldon). You may go ahead.

(Susan Sheldon): Thank you for taking my question. And, Dr. Stenzel, thank you so very much to you and your colleagues at the FDA for working so hard. I didn't realize that the workload was so heavy.

And at this point my question, I'm thinking that I have no hope. But I'm going to go ask the question anyway.

We submitted a Q-Submission for a flu test. And we were encouraged to do that and we did. And the test is a de novo test because it's a software as a medical device and we needed feedback from the division.

And the division turned around and said that we don't have time to review it. If you want us to review it, send it back again and we will take 121 days to do that.

This happened in mid-November. And I was wondering if you see any light at the end of the tunnel when other tests like flu at this point, because the season is coming up and we're hoping to do the clinical trials at that point.

When can we submit this Q-Submission for a de novo software as a medical device? Any light in sight?

Dr. Stenzel: Yes, so it's a de novo. It means there's no predicate...

(Susan Sheldon): Right.

Dr. Stenzel: ...out there. And we would determine whether it can be down classified to Class 2 in the de novo submission.

The challenge we have is we have begun putting on hold full MDUFA submissions, full regular non-COVID submissions. And as I just explained, we probably would start - if we start to see a high volume of COVID transition, you know, to full submission, we would more than likely have to put them on hold.

And we have put over 100 regular non-COVID submissions on hold right now. And that is weighing on us. We want to get back to them as soon as possible.

So what we have done is the surge did not move all reviewers of IVD products into COVID, but it certainly put a large number there.

But we are continuing to review some MDUFA full applications. Those that we don't put on hold, unfortunately due to the workload that we have, those MDUFA files in most cases will move forward more slowly.

We have, you know, tried to come back to those MDUFA files as soon as possible. You can continue to submit the pre-sub following our

recommendations. I guess it was 120 days. If our staff have capacity when it comes back in, we can try to address that.

And if we do take it up, in all likelihood it's not going to meet our pre-pandemic timelines that we were holding ourselves to and our office was highly successful in meeting our MDUFA timelines.

But with this workload, we're doing our very best. But those non-COVID files that we pick up are going to obviously move more slowly.

When you submit, we will, of course, respond in some way telling you what our current situation is and giving you our best time estimate on when we maybe can get to it or further instructions.

We're doing the best we can. In the case of something that is a de novo, you can consider a breakthrough request. If it is a novel technology and they qualify for a breakthrough we are meeting our breakthrough review timelines.

We are meeting our IDE submission timelines. So we have not stopped handling breakthrough requests for non-COVID. We're not encouraging breakthrough requests for COVID because they are EUAs and we're already trying to work fast to get the authorization on those.

But for non-COVID submissions such as this, that would be de novo and may likely fall into a breakthrough category that we can consider.

(Susan Sheldon): A breakthrough particularly because it's a novel methodology, novel technology?

Dr. Stenzel: Yes.

(Susan Sheldon): Okay.

Dr. Stenzel: So look into the breakthrough guidance to see if you meet the breakthrough conditions. If you do then, you're open to filing a breakthrough application for designation.

So even though we're meeting our commitment to review the breakthrough request and make a decision, a timely decision, according to our commitments, once we do designate, we are not able to keep up with all other time commitments related to breakthrough. But it will be assigned a reviewer in those cases if you are designated.

All breakthrough requests get assigned a reviewer as IDEs. We will work through that according to our stated objectives. We'll make a designation decision.

And then after that you will be assigned a reviewer and then after the time commitments that we've made in the guidance will be difficult for us to follow.

But you will have a reviewer and those pre-subs for breakthrough will be followed-up on.

(Susan Sheldon): Okay. So if we don't qualify under that guidance document, because the technology is novel and it's de novo, but if we don't qualify under those guidelines as a breakthrough device, then you suggest we go ahead and submit a second sub-Q like they have told me and hope for the best. Is that correct?

Dr. Stenzel: Yes.

(Susan Sheldon): Okay. Thank you very much.

Dr. Stenzel: We'll get back to all submissions as soon as possible, but the volume is overwhelming.

(Susan Sheldon): Yes. I understand. And my hat goes off to the colleagues at the FDA. Thank you very much.

Coordinator: Our next question is from (Brandt Mittler). You may go ahead.

(Brandt Mittler): Hi, Tim. I'll try to be brief. Two questions about neutralizing antibodies. In terms of the PRNT methodology, does the FDA have a list of laboratories or entities that will perform validation studies for a commercial manufacturer?

And Number 2, both last week and today, you made comments about the specific claim regarding neutralizing antibodies, talking about it's dangerous to claim immunity. I understand that.

But what is the appropriate claim with regard to neutralizing antibodies in terms of how it should be phrased? Thank you.

Dr. Stenzel: So we have authorized to my knowledge one neutralizing antibody test. You can look to that labeling and see if it matches up with your test. So that would be a good, you know, something to follow.

It's our current stated public, you know, thoughts in essence around neutralizing antibodies. And, again, we do have more extensive thoughts that if someone emails us to the template's email address and asks for our current

thinking on neutralizing assay validations and recommendations, our review staff can now provide that with up-to-date thinking on that.

(Brandt Mittler): Okay. Does that include -- thank you -- a list of entities that provide the PRNT methodology validation?

Dr. Stenzel: I'm not aware of entities, but our neutralizing antibody team is very good. And they would know better and are likely to have some suggestions.

So if that comes in through the template's email address asking for recommended PRNT assay providers, that will go to our serology review team and hopefully we can give you some specific guidance there.

(Brandt Mittler): Thank you.

Coordinator: And our next question is from (Autumn Colossius). You may go ahead.

(Autumn Colossius): Hi, yes. Thank you. My question is a follow-up to one of the previous questions and entirely related to the 90 day hold period or the 90 day reallocation of resources on the FDA review side.

Does the FDA at this point in time anticipate any additional reallocation of resources beyond the 90 days originally attributed to, or pushed through, this EUA bullet?

Toby Lowe: Tim, if you're speaking, you might be on mute.

Dr. Stenzel: Oh, you're absolutely right. I'm on mute. The large volume of applications we're still receiving is a little bit unexpected perhaps. But we were hoping for

more trickle than this. And so some files are coming off hold. You're talking about regular non-COVID submissions.

I know of a handful that have now started coming off hold. That will continue but it won't necessarily be a large volume. So we, on a rolling basis, will be providing updated information.

And if someone has been held, say, for 90 days and they're getting notified again, the next phase of notifications if they've been held the full 90 days will be more definitive as to when - by when they will receive a reviewer.

So we may have some extension of holds, but the second round of extensions will have a time commitment for when you will receive a reviewer and the review will begin.

But as I've said earlier in the call, we cannot promise our usual good performance on MDUFA turnaround times in this current situation. We'll do our best, but we can't promise anything.

(Autumn Colossius): Thank you very much. We certainly understand the workload that you're going through. So we appreciate all the work the FDA has been doing on our behalf so thank you.

Dr. Stenzel: Yes. We do want to get back to those MDUFA applications. And we're not going to put anybody on indefinite hold. The second round of holds related to this will have a stated timeline for when you will be assigned a reviewer.

(Autumn Colossius): Thank you.

Coordinator: And that concludes the question-and-answer session. I would now like to turn the call back to Timothy Stenzel.

Dr. Stenzel: Actually, Irene.

Irene Aihie: Thanks, Tim. Thanks, operator. I appreciate that. Thank you. This is Irene Aihie. And we do appreciate your participation and thoughtful questions during today's town hall.

Today's presentation and transcript will be made available on the CDRH Learn Web page at www.fda.gov/training/cdrhlearn by Friday, January 22.

If you have additional questions about today's presentation, please email cdrh-eua-template@fda.hhs.gov.

As we continue to hold virtual town halls, we would appreciate your feedback. Following the conclusion of today's virtual town hall, please complete a short 13-question survey about your FDA CDRH virtual town hall experience.

The survey can be found at fda.gov/cdrhwebinar. As a reminder, there is no town hall next Wednesday, January 20. We will resume our town halls on Wednesday, January 27.

Again, thank you for participating and this concludes today's virtual town hall.

Coordinator: And this concludes today's conference. Thank you for participating. You may disconnect at this time. Speakers, please stand by for post-conference.

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