FDA Virtual Town Hall Series –
Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests
Moderator: Irene Aihie
June 10, 2020
12:15 p.m. ET

Coordinator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode 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 like to inform all parties that today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn the conference over to Miss Irene Aihie. Thank you. You may begin.

Irene Aihie: Hello, I am Irene Aihie, of CDRH's Office of Communication and Education. Welcome to the FDA's 12th 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, Sara Brenner, Associate Director for Medical Affairs, and Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and Radiological Health, all from CDRH, will provide a brief update. Following opening remarks, we will open

the line for your questions related to today's discussion. Please remember that we are not able to respond to questions about specific submissions that might be under review.
Now, I give you Timothy…

Timothy Stenzel: Thank you and welcome, everybody, to this town hall today and look forward to the questions and helping out any way we can there. I wanted to talk about a couple of key topics first. One is prioritization of reviews.

So we have - these are unprecedented times and we've seen unprecedented submission. I calculate that the virology branch within our office -- which handles the EUAs for SARS-CoV-2 and COVID -- has seen the workload just for EUAs, not the PEUAs and not any other communication that is 60-folds greater than their usual submission volume.

This is, of course, why updated our guidance with the notification pathways so that once developers have validated their tests and if an EUA is required that they can notify us and then once that's been confirmed we'll add them to the notification list and they can market their test in the U.S.

And there are certain categories that do require prior EUA approval and, of course, we prioritized those and those would be home collections and home testings.

Another prioritization that we make are for anything that is high throughput. We typically define high throughput as having a batch size of, let's say, 200 or more tests per batch so that those applications obviously have - as all do, but also has significant public health importance because they allow us to get testing done more quickly and more efficiently.

The other category that we placed a very high priority on are the point of care tests and any of it - for any of the types of tests that we authorize.

So we do have this relatively small staff of virology expertise that manages our usual workload and which is sufficient for that. We are not staffed for an emergency such as this type.

Now, we have added to that, more than doubling our review staff and bringing in strong, scientific support for other areas in health.

It is our goal to authorize every EUA as soon as possible as long as there are no issues. We review applications when they come in.

We make sure that there aren't any issues and we prioritize them based on the priorities that I've already mentioned.

If there are no issues with the application and they are not in one of the high priority categories, we do let these developers know that we have received their application and that basically due to the volume of applications they will get to them as soon as possible, but in those cases a substantive review hasn't begun.

And we - for those that are eligible through the notification pathway to be marketed in the U.S., we do our best to make sure that everybody knows, but if you fit in that category and you notify us and we acknowledge that, then you're allowed to go ahead and market.

So that's how we've dealt with this overwhelming workload and we know that there's a lot of interest in getting EUA authorizations finalized as soon as possible.

Next, I wanted to move onto an important topic as hopefully over time the number of patients who have been diagnosed with COVID and therefore have samples that would be corrected and could be utilized for test developments and validation that if you see yourself developing an assay and need those - patient samples in order to pursue your validation tests and even perhaps development tests, we would urge you to begin collecting and perhaps banking those samples appropriately, of course.

And if there is anything related to stability of samples, that could be an issue ee would ask you to reach out to the template's email address so that we can address any potential stability issues in storing those samples, but we are going to be open to the use of these banked samples for not just EUA applications and validations, but also conversions to usual full authorization. Okay. I think that's maybe all that I'm going to cover right now.

So I'm going to turn this over to Toby who has a few updates. Thank you.

Toby Lowe: Hi, everyone. Thanks, Tim. So I just wanted to give a couple of updates on some recent information that we've put out on our Web site.

We discussed a little bit last week about issues with certain transport media being incompatible with certain testing platforms and late last week, we did issue a letter to health care providers regarding that issue specifically talking about the issue of using transport media containing guanidine thiocyanate or similar chemicals with the Hologic platforms or with other tests or processes that use bleach due to the risk of producing cyanide gas.

That letter to health care providers, really to labs, can be found on our Web site. It's also linked from our FAQ page if you look in the What If I Do Not Have section of the FAQ and specifically in the first question under that section

which is about swabs and media.

There's a link to that letter in that section. We also updated that question. We streamlined the answer to focus on the types of swabs and media rather than looking out for specific catalog numbers as we had previously.

And going along with that update, we also linked in that same section of the FAQ's as well as in the blue box at the top of that page.

We put out a PowerPoint presentation that is a tool for labs and other stakeholders to use to determine the best testing supplies substitution strategies.

So sort of a mix-and-match PowerPoint tool that focuses on the different areas that we have already included in the FAQ's in that what if I do not have section. It just provides another resource to see what are some of the different compatibilities are there.

Also on the FAQ's, we added a section to the FAQ with questions about 3-D printed swabs and we may have mentioned this previously on this call, but we also added a section about data reporting for labs to report to public health authorities.

And also relative to that, last week HHS issued a guidance on the CARES Act laboratory reporting requirements. They put out a statement about that and a guidance document with corresponding FAQ's up on the HHS Web site.

And lastly, at the end of the week last week we put out a new Web page that includes data from the independent evaluation of COVID-19 serological test.

So we previously talked about the independent evaluation program mostly

being done at the NCI labs for serology tests and this new Web page -- which was also linked from the blue box at the top of the FAQ page -- provides some of the - or provides the data for the tests that have been - that have gone through that program.

So I think that's all of the updates that I wanted to make sure to flag at this point. And so I can turn it back over to Irene and we can get started with questions.

Irene Aihie: Thanks, Toby. Operator, we'll now take questions from our participants.

Coordinator: Thank you. We will now begin the question and answer session. We ask that you limit yourself to one question only, please. If you would like to ask a question, please press Star 1, unmute your phone and record your name clearly.

Your name is required to introduce your question. If you need to withdraw your question, press Star 2. Again, to ask a question, please press Star 1.

Our first question will come from (Mark Hackman). Your line is open. (Mark), we're not able to hear you in conference Be sure to unmute feature on your phone.

(Mark Hackman): Can you hear me now?

Coordinator: Yes, thank you.

(Mark Hackman): Okay. Good morning. Thank you for taking my call and thank you for having these town halls. They've been extremely helpful to the industry.

My question is related to fully home testing and what I - my question is related to that currently there's 1.6 million people living with Type I Diabetes in the

United States, approximately 200,000 of them are under the age of 20.

These people are required to test their blood multiple times a day for the blood glucose levels. We are wondering when a fully at-home test will be available because we feel that the fully home - fully home tests are much safer, they reduce the need for PPE's.

The fully in-home tests are faster, they're much faster than the big box test. They're usually done in 15 minutes results. Fully in-home tests are much more distributable than the big boxed tests and they're also 2 to 10 times less expensive than the big boxed tests.

So my question is when might we expect to see an EAU for a fully at-home testing? Thank you.

Timothy Stenzel: Yes, thanks, (Mark). As I stated earlier that in-home testing and home collections is a top priority.

We are working on specific recommendations for developers, but for in-home testing. But, of course, are willing to engage with them right now, you know?

We have a number of interested parties. It is important to make sure that in that setting that all aspects of testing are accurate from appropriate use to appropriate collection of sample, appropriate processing and appropriate reading of those results and interpretations.

We're very open to assist, have assisted testing in the home done with telehealth, which maybe mitigate some of the potential risks for in-home testing.

So we are very open to it and as soon as we have a complete application, that application will be processed as long as everything looks good, in very short order.

(Mark Hackman): Great. Thank you very much.

Coordinator: Thank you. Next, we'll hear from (Arianna Hawkins). Your line is open

(Arianna Hawkins): Thank you for taking my question. So on May 22nd, a manuscript by (Bullard, et al), was published online through the Clinical Infectious Disease Journal and that article demonstrated that specimens collected after 8 days of symptom on-set or with CT values less than 24 could not be cultured and this suggests that those specimens are not infectious.

So my question is how would you expect this information to affect patient management recommendations and future point of care assay performance requirements?

Timothy Stenzel: Yes. So I'm familiar with that paper and I read it. It's interesting. There are some challenges when you culture a virus and it may not culture all viruses, but I think there's a couple of really good takeaways from that paper.

One is that it does kind of chart on what the viral level course through infection to resolution, perhaps of symptoms.

There is - this is a place where science is still evolving to determine even, say, long after or just after symptoms resolve if there's detectable nucleic acid or genetic material of the virus in a patient sample, what is the meaning of that?

I think as we begin to learn more about immunity and as we have patients be

tested and confirmed with serology tests and as we start - are able to start, say, authorizing - neutralizing antibody tests and we're very open to accepting and neutralizing antibody tests, which, of course, will add information about whether the antibodies that have been raised to the virus by patient are actually able to impact immunity.

So this is still an evolving area and if someone remains positive, say, by virus after they incubate the 7-day period and their symptoms are resolving, you know, what does that mean as far as the chance for them to potentially infect somebody else, potentially relapse. Those are still open questions and we do track that science very closely and - because we do get asked on a fairly frequent basis on the FDA's opinion on how this information should be used for public health purposes. Thank you.

Coordinator: Our next question is from (Jackie Chen). your line is open. (Jackie), we're not able to hear you in conference. please check the mute feature on your phone? Not hearing your response. We will move forward.

Our next question will come from (Mishayla Hoffmeyer). You may go ahead.

(Mishayla Hoffmeyer): Yes, hi. Thank you for taking the time to put these town halls together. Again, they're very much appreciated.

My question is concerning - and I appreciate the at-home guidance and the new EUA template. My question is concerning asymptomatic screening for return to work with an at-home collection.

Can you comment on how we could reconcile asymptomatic screening with at-home testing?

Timothy Stenzel: So it kind of depends on if the at-home testing is by prescription or is over-the-counter. There's…

((Crosstalk))

(Mishayla Hoffmeyer): We would do prescription.

Timothy Stenzel: ... prescription - pardon? You'd do prescription? So if a test is authorized for testing on patients who are suspected of having COVID-19 and there is an order for that test by a health care professional.

Then that is covered for a - we, you know - we say that the testing for the asymptomatic person, we would want that result to be reported out and utilized as appropriate.

So hopefully that addresses your question.

(Mishayla Hoffmeyer): Thank you.

Coordinator: Thank you. Our next question will come from (Yayir Black). Your line is open.

(Yayir Black): Thank you so much for taking my call. I was wondering in regard to the scope of the testing by high complexity laboratory.

According to the CLIA regulations, tests are modified from the approved manufacturer instruction, are categorized as high complexity. Does that mean that a high complexity lab has the ability to deviate from the indications of use for the device?

For example, the high high complexity lab be able to perform a COVID test

using salivaif there are authorized COVID detection assays that do not include saliva.

Timothy Stenzel: Yes. So we have recommendations in our templates, in our molecular templates, about the use and - of saliva and our recommended validation of saliva.

Just to remind listeners that saliva in our reviews have had variable performances and there are some that we have - when they have come in for EUA authorization that we have not been able to authorize due to inferior performance.

So we feel like saliva is a sample type. It is a very important specimen to validate properly and ensure that we're getting accurate results with saliva in comparison to a usual swab-type sample.

As far as what high complexity labs are allowed to do, on our FAQ page we state that labs can validate sample types that have already been authorized and we have confidence that they can be validated to be performed accurately and, you know, as long as the underlying test that they're using has an EUA authorization, then the modification to add saliva is acceptable as long as your validation shows that it performs well.

We encourage clinicians, but it's not required for high complexity LDC labs to make that kind of a modification to an EUA test.

(Yayir Black): Would that include other novel specimen collection other than saliva, for example?

For example, a novel all-nasal wash or some kind of other type of specimen that

may be collected from the areas of the mouth ?

Timothy Stenzel: So we've authorized nasal washes. Oral fluid is really in the same category as saliva. So however you collect that oral fluid, saliva, as long as you validate it and it performs well, you can use the saliva recommended validation to guide you.

(Yayir Black): Thank you so much. I really appreciate it.

Coordinator: Thank you. Our next question will come from (Jessica Wasserman). Your line is open.

(Jessica Wasserman): Hello. Thank you. Especially excited about your prioritization of the POC and so forth.

Along those lines there is our one template in draft form that's been distributed on the POC, but I just wonder if there is - that's going to be changed? It mentions specifically that it's for lateral flow and I wonder if that's the way you're going to go forward with that?

And then also if there's anything you can say about the sort of distinction between POC and the CLIA waived and telemedicine and at-home just to get those distinctions in terms of the applications more clear? Thank you.

Timothy Stenzel: Yes. I believe our POC recommendation for validations are in at least one of the templates and they're pretty identical to one another and just assure that in a health care setting that lay users which we design is non-laboratory trained personnel, you know, nurses, physicians, allied health folks who are normally doing the testing in that setting - for that POC setting.

That the test be shown to be accurate when they perform the test, only with the instructions that come with the test and without any specific training, of course, to be able to have a lay user get an accurate result does require perhaps some additional developments at least of easy-to-read instructions, but also the work flow related to the work flow.

If there's any user interface for that test or there's any chance of variability such as volume, such as time, et cetera, and those particular kinds of different categories are outlined in the template briefly, but they're given there.

Then we look to flex studies around those time point conditions to show if that particular essay or test is - and the instructions for use for that are anywhere near a point where accuracy may go down if you go, you know, too long or too under time or too much or too little of volume in a lay user population.

When it comes to other environments OTC or home, there's two kinds of home. There's prescription home and there's OTC, or over-the-counter.

We've seen the involvement of the health care provider in writing an order and being involved in the test and selecting for what tests and when a test should be performed and reviewing the results and guiding many patients through on what to do with those results.

Perhaps there's follow-on testing that would be helpful. Perhaps a recommendation on isolation or other situations.

So when a clinician or health care worker is involved, that does mitigate some of the risk versus a completely over-the-counter test -- which we are open to -- but may require additional accuracy testing when a health care provider is not involved.

So as far as CLIA waiver, if a test is going to be performed outside of the high complexity lab situation, then it does require EUA authorization to render the test by our office and we determine if that test can be performed outside of a CLIA - a high complexity CLIA waived environment and we will note that both in our authorization and in on the listing on our Web site as either M for Moderate or W for Waived.

Frequently, a test that may be used for home or for a non-health care environment situation with non-health care workers performing it, typically a developer might go through a point of care authorization demonstrating that lay users - lay health care users can accurately do it on the way to delivering something either by prescription to the home or over-the-counter. Hope that helps.

Coordinator: Thank you. Next, we will hear from (Grant Mitler).

(Grant Mitler): Yes. Tim, this is kind of a political question. I've been meaning to ask you this now for several weeks, but it's prompted by the House hearing yesterday where I guess the FDA was - not I guess - the FDA was slammed again by Representative Christian (unintelligible) who's been after you all for weeks.

The problem is this: We know that these, for example, the rapid antibody test that you all have developed, you know, extensive templates and processes by which I believe many manufacturers have submitted samples to the NCI, have submitted mountains of data, some from China, for example, some from the United States in that with validation studies and in general it seems to me from having seen quite a bit of these data that people are acting in good faith.

But if you listen to the representative and many, many other critics, many from large medical school labs that are developing competing studies, you would

think that the - this whole process that you're presiding over is one of crooks and, you know, bad intentioned people.

Is there anything that your office can do to assure the public that the people that you're dealing with and the tests that you're evaluating are - these people are operating in good faith and that they're not trying to develop fraudulent products for the public.

Timothy Stenzel: Yes, I would say publicly that we always assume good intent and - with developers and there's clearly with some tests there have been reports and we have seen issues where that particular test does not perform well enough to be authorized.

So we take a very even-handed approach. We look at all the data. The NCI effort, we believe, is a great one because it not just assures the FDA of the accuracy of tests that go through that program, but we make those NCI test results public so that others can see for themselves the performance of those tests.

So we believe that sort of unprecedented transparency with this process will address a large number of the questions. So I do hear what you're saying and we're doing our very best in that category, in that area.

Coordinator: Thank you. Our next question will come from (Craig Benson). Your line is open.

(Craig Benson): Yes, thank you for taking my question. I'm wondering if a company receives a EUA or is listed on one of your lists as an appropriate test to be used decides the change, the test name or is - or needs to change the test name, is there a mechanism for that to occur?

Timothy Stenzel: I'm sure there is. (Toby), may be able to answer that question. There are certainly clear reasons why a test might need to be changed. There likely would be some official paperwork unfortunately, but (Toby), can you address that question?

Toby Lowe: Yes. Yes, if a company has to change the name for their test, we would just ask them to reach out to us. They can do that through the EUA mailbox or if they are working with a lead reviewer, they can go directly to the lead reviewer and we can work through that process with them.

(Craig Benson): Thank you.

Coordinator: Thank you. Next, we will hear from (Tom Slovak). Your line is open.

(Tom Slovak): Thank you for all the great information you've been supplying with these weekly calls. This is my question. Given the large EUA backlog for those who are waiting EUA approval for COVID-19 stereological tests in their Part D list, what confidence can you give us that imported shipments of these tests can clear Customs smoothly prior to the EUA being granted?

Timothy Stenzel: So if you're on the notified list and you're having any struggles with getting those tests into the country, reach out immediately to the EUA template email address and we have folks who we rely on to address import/export issues in an expeditious matter.

So we have that pretty streamlined as long as it - that there's no issues with the notification that there shouldn't be holdups, but if there are, we will work through them in short order. In my experience that I've observed, this is usually resolved.

If there are issues, there usually aren't, there aren't that many, within 24 hours. Thank you very much.

Toby Lowe: And I would just also note that our import folks are looking at whether the customs notification list and also whether it's labeled - excuse me - whether it's labeled according to the guidance. So that's something to keep in mind when you're working on the test to make sure about the labeling, not just what's in the guidance and that will help streamline the process as well.

(Tom Slovak): Great. Thanks.

Coordinator: Thank you. Next, we will hear from (Thomas Roder). You may go ahead.

(Thomas Roder): Great. Thank you for taking my call. This is sort of a follow-up on a prior question. There are two issues on import/export from China. Import, obviously, once it gets to the United States, the FDA has done a great job of giving us guidance on coding for the initial importers.

The problem that a lot of us are experiencing are on the Chinese side and this comes in the wakes of the FDA's change in policy regarding thermology tests and when you can distribute. On the China side, they now have as of the last week or two what they call the White List and the Black List, and these are for Chinese exportations inside China.

When you're trying to get your test kits out, they look at this list and if you're on the black list, those tests are primarily the ones that the FDA has provided notice are no longer available distribution. The white list is supposed to be for test kits that are able to be imported in the United States.

The problem is that white list is not comprehensive. A lot of the test kits that don't have EUA's, but are allowed for distribution in the U.S. are not being allowed out of China. I've had conversations with other distributors like myself that are having this problem and my question is are you aware of the Chinese white list and black list? Is there anything that you guys have done or can do to help us facilitate that process?

Because the Chinese government is essentially not allowing out any test kits that don't already have an EUA even if they're allowed the distribution in the U.S. Thanks.

Timothy Stenzel: Yes, we are aware of those lists. Yes, we do our best. We have worked with our international colleagues, in particular, those in China, to address this issue and we have international experts within the center at the FDA

who have worked hard on this issue and certainly have tried their best and made some progress. I have personally when called upon helped out get those developers on the white list when my help could help those companies and there is the ability to be on the white list while you're still in development and may want to do the validation testing in the United States, which, of course, we would support.

And that - those have limits on the amount of tests or kits that can be sent at a given time. So we recognize the limitations there. So I - it's - if a test is on the notified list and is allowed to be marketed in the U.S. and you're having export issues in China, send us information onto our template email address and we will certainly raise it to our colleagues within the center who help us deal with that particular issue and we'll do our best to help out.

(Thomas Roder): I appreciate that. If I can, a quick follow-up. I'm talking about specifically

importers like myself who are dealing with test kits that have been in the EUA process are since the beginning of April and it appears that the Chinese are putting on the white list only the EUA-approved test kits.

And so yes, we've been in the - we are into the validation process and has been for weeks now, but there are several other importers like ourselves that are dealing with manufacturers that have long (long ago filed the EUA and were actually listed on the FDA's Web site of authorized manufacturers that are in the EUA process, but somehow we're not making it onto the white list.

Timothy Stenzel: Yes. No, we're aware of that issue. I have some specific information that folks can get on the white list, so who haven't been EUA authorized in the U.S. So I can't speak for the Chinese process at all. I can just speak to our process of trying to - and to help out the situation as best we can working with our Chinese counterparts to address these questions.

So we are strongly supportive of the tests that has been notified in particular of being able to be utilized in the
United States and would support every effort to get it from country of origin to the U.S.

(Thomas Roder): Great. Thanks for the call and I'll - we'll reach out to you directly on this issue.

Timothy Stenzel: Thank you.

(Thomas Roder): Thanks.

Coordinator: Thank you. Our next question comes from (Ken Kim). Your line is open.

(Ken Kim): Hi. I'm a physician and actually quite involved in the clinical trial space. My

question revolves around antigen. I want to know how many companies that you - the FDA is aware of that is developing antigens that already applied for EUA for antigen.

And I'm aware of the (Clodel) EUA antigen approval. The reason why I ask that is I wanted to get antigen to actually use that as a diagnostic tool of (Clodel), but then they wanted - they're mandating their contract that we have to exclusively use (Clodel) and cannot replace it for the next three years unless there's a double-blind randomized trial showing this other agent head-to-head is better.

And I said, number one, most things are going to be EUA-approved. Number two, no one's going to do a head-to-head to the initial trial and three years is ridiculous.

So basically, wanted to create a monopoly to lock in people and it's very frustrating and I'm actually a little worried that a (Clodel) person that's on this phone will also retaliate because now they will not even - they won't sell me kits because I won't sign that if we supply.

I was wondering is the FDA allowing that to happen and is there any way you can actually lock other people out with that kind of language?

Timothy Stenzel: Let me just make sure that I understand your question. You want to obtain antibodies or antigens?

(Ken Kim): Antigens for...

Timothy Stenzel: Antigens?

(Ken Kim): ... for a serology test. No, antigen, not serology. Antigen is different from

serology, right?

Timothy Stenzel: So the antigen…

((Crosstalk))

Toby Lowe: You're looking to use the actual antigen test? You're not looking to source the antigen ; is that correct?

(Ken Kim): Correct. When we want to use the antigen test for diagnostic purposes and there's only one FDA EUA-approved antigen, to me as a physician, I've been doing clinical trials of one over 700 clinical trials, antigen is going to be a very good screen test that could actually replace TCR for screening, but we need more antigen tests. I think we need more antigen tests, not antibody tests.

So I've requested (Cordel)...

Timothy Stenzel: Okay. Okay.

(Ken Kim): ... to use this. Yes. So...

Timothy Stenzel: Okay.

(Ken Kim): ... I have two questions…

((Crosstalk))

Timothy Stenzel: So you're having trouble acquiring those (Cordel) tests?

(Ken Kim): Yes. Well, because they're refusing because they want me to sign a contract that

says that I would not go to a different antigen test if something comes up for three years unless there's a double-blind randomized trial head-to-head against their antigens, which to me is not - to me, I think, is not right in this emergency environment.

So they are using their EUA to actually, you know - I'm at a standstill because I would like to buy their - I'd like to buy lots of their kits, but they won't sell them to me because I won't sign that.

Timothy Stenzel: Okay. I understand better. Thanks for explaining that.

(Ken Kim): Yes. So that's the problem. It's really frustrating because, you know, on the fields we definitely want to use this as a point of care test. It's great. But I don't know whether this is legal for them to take an EUA and actually create a market lock that anyone who starts using these we're locked in with them for three years. We can't use another antigen test when another one gets approved. You see what the problem is?

Timothy Stenzel: Yes. Yes, no, I see. Let me note this and we'll look internally at this (unintelligible)...

(Ken Kim): I can talk offline.

Timothy Stenzel: Yes, talking offline may be helpful too.

(Ken Kim): Yes. I - you know, I think - I typed it up in the email. So if you email me, I could set up a call, we could talk about it and I could send you the language, but I think it's a problem because that shouldn't - that - we're trying to actually do good things for the country in terms of diagnosing disease and you can't get situations where someone is going to lock you into something that, you know,

isn't really credible. Three months from now there will be another antigen that might be better and we can't - we wouldn't be able to switch to it legally.

Timothy Stenzel: Okay. I certainly hear what you're saying and understand what you're saying and, you know, it's probably best if internally at the Agency we look into this and talk with you further.

There's a lot of listeners on this call and, you know, there's obviously a good bit of transparency that goes on because there's a lot of listeners on this call.

So - and we make ourselves available right now week in, week out here on this call. So I appreciate your calling. I would just add that we're very interested in additional antigen tests to be authorized.

There seems to be a real shortage of developers in this space. So I would encourage anyone who wants to develop an antigen test, that's - they come talk to us and let's see what we can do because we are very interested in adding to the number of antigen tests.

Coordinator: Thank you. Our next question will come from (Shanivas Natribody). Your line is open.

(Shanivas Natribody): Hi. Thank you so much for taking my question and thank you for all that you are doing for our country and for this pandemic.

Gentegra? has developed a guanidine sinus (unintelligible) and saliva media and the saliva media that we have developed does not dilute the sample.

And in our preliminary in our data nasal samples you see that the viral transport media for naso-pharyngeal swabs that are collected at the same concentration as

the viral load in the saliva match up.

So what we want to do now is I'm looking for head-to-head testing of our media against a standard camparent media that is on the market, but I'm having a hard time getting clinical samples that are collected in my media because most of them get collected in the standard VTM's and the standard saliva tubes that are out there.

So can your office - my question is can your office in some way help me out or help me get connected to acquire these samples so that I can test them?

Timothy Stenzel: Yes. So unfortunately, the FDA doesn't directly collect and store patient samples. I would think that there would be a number of potential academic collaborators, if not other developers.

You know, there are - we have authorized some labs already for saliva collection with devices and they're on our Web page. And so it would be a first spot.

(Sara) sometime has to drop off I forget if it is this call and the next call. (Sara), are you still on? Can you potentially address this and maybe potentially hitch this developed up with (unintelligible) others?

Toby Lowe: She did have to drop off.

Timothy Stenzel: Okay. If you send us an email to our EUA template email address, we will see if (Sara) can't help out with making some connections here, okay?

(Shanivas Natribody): That would be wonderful. Thank you so much, Dr. Stenzel.

Coordinator: Thank you. Our next question comes from (Brad Apple). Your line is open.

(Fred Apple) Hi. Hope you can hear me okay. Thanks for taking my call. It's actually (Fred Apple). I'm a clinical chemist at Hennepin county medical center in Minneapolis doing clinical work on antibody testing, as well as, applied research.

My question is addressing the calculator that I see that the FDA puts in there in the latest interim guidelines for COVID-19 antibody testing from the CDC and my question is dealing with this orthogonal testing which has been confusing some of us to the idea that you do one test.

And I see some laboratories, mostly reference labs, are doing a second test before they record a positive antibody test and it doesn't really explain carefully enough or implications of whether you're looking at the *capsid??* or are you looking at the spike protein.

That's, I guess, like, the general, I know I said this three times. The general of our question, the FDA is not requiring two tests before a report's put out. That's a lot. Any way you can comment on any of those things?

Timothy Stenzel: Yes. Yes, absolutely. Well, we developed that calculator within our office to try to help in this situation. Particularly, even with high specificity tests, single tests, high-performing tests where prevalence might be low, below 5% -- which probably is true in large areas of the country fortunately still -- that a positive doesn't have always a great positive prediction value.

So we in our - we work for the CDC on serology guidance or recommendations. Not sure if it qualifies as guidance in legal terms. I think recommendations that we recommend that in appropriate situations where it's important that you

confirm a result with a second serology test.

We do not require that in our EUA authorizations, so we try to stress that it should be a different serology test and we - there may be tests that look at different parts of the different proteins even though it might ultimately target the same protein if it targets different parts of that protein that may be enough obviously having the spike in an (unintelligible) an-protein is clearly two different tests would be the easiest for providers to assess.

So we have asked and are requiring that this information be present to the instructions for use and we certainly, I think, can look at whether we can make this information a little bit more transparent on our Web site so it's easy for clinical folks to extend laboratory folks to take a look and make recommendations about if you're going to do a (unintelligible) test what is it.

What's interesting is that even if you have an authorized test, it has the specificity above our bar, if you combine, you know, two say 95% specific assays together that are different orthogonal, you end up even as the lower predictive population it's having a fairly decent positive prediction value. I hope that addressed your question.

(Fred Apple): As forensic toxicologists too, we're using the word, "confirmed" is, I guess, concerning in the context of we all know that what are we confirming at least on the times of the blood draw?

So I guess I - some of us that were concerned about that were confirmed because if it was early versus late and we know individual to individual immunogenicity is not the same for everyone for getting antibody titers, so any thoughts about that word? Because it's a powerful word and some people are using it like it means it's just dogma. Does that make sense?

Timothy Stenzel: No, I understand your concern because - and this is partly why we provide the calculator because even if you have two extremely high specific tests, it's not going to ever reach, you know, the specificity of 100% even if you require two positives.

So there will always be a chance that it's still a false positive.

(Fred Apple): I agree. All right. You heard my concerns. Thank you. I appreciate your input.

Timothy Stenzel: You're welcome.

Coordinator: Our next question will come from (Eric Clock). You may go ahead.

(Eric Clock): Hi. Thank you for taking my call. My question is also related to at-home testing. So we're currently evaluating saliva sample collections for at-home testing.

We appreciate that the FDA released a safety warning last week regarding the transport media containing guanidine given that there's a risk of exposure for the cyanide gas in reaction to bleach, but I know that you guys noted the risks there during the clean-up settings in a laboratory setting, but is there a - is there the same risk present for the home collection devices that are using guanidine thiocyanate?

And then should similar warnings and advisories be released in case there's a spillage at home with the risk of bleach interaction?

Timothy Stenzel: Yes. So we realize that guanidine alone and not in connection and/or in mixing with bleach in and of itself is a toxic chemical and when we authorize a home test, a home collection rather - and I think we've only authorized one so far that

has guanidinium in it - it is the device that blocks exposure to the chemical.

In that particular case, the chemical is only in contact with the sample after a sample is taken and the device is closed and in closing the device and releasing the chemical it prevents - it locks the cap and prevents leakage and prevents access to that at that point.

So at least in the home collection situation we seek to only authorize collection methods that we deem to be safe and we do consider that sort of situation in particular with guanidinium.

There could be a testing situation in the home where that may be an issue and you highlighted an important safety consideration that we want to keep in mind, but it would be odd that a saliva sample collected at home for home testing wouldn't necessarily go through guanidinium straight onto the device and not need guanidinium in the sample.

(Eric Clock): I'm familiar with that device. There is still potentially an inherent risk that, let's say, the cap is pierced or stepped on, you know, in that event there is still a risk of, you know, potentially at-home spillage. Is there any comments there regarding what the FDA recommends for clean-up in an at-home setting?

Timothy Stenzel: Well, we are not aware of data that suggests that there could be spillage. So you highlight an important safety signal that we will look into.

That was not our understanding on the safety performance of that device. So (Toby), if you're still on, I know you've been dealing a little bit with this issue. Do you have any further thoughts?

Toby Lowe: Yes. Well we will look into this a little bit more. I'm looking quickly to see if

I can see if it was in the directions, but we're going to have to look into that further.

Timothy Stenzel: Thanks for pointing that out. We will definitely look into it and investigate it and do what's important for public health.

(Eric Clock): Thank you.

Coordinator: Thank you. Our next question comes from (Brandon Walker). Your line is open.

(Brandon Walker): Hi. Just wanted to start out and thank the FDA for their extraordinary measures hosting these weekly town halls.

My company, (Chameleon), has developed a rapid self-administered SARS-CoV-2 diagnostic for at-home testing using saliva. We're starting clinical trials in the next few weeks and preparing the EUA, but we need a little further guidance.

This is a proprietary sample to (unintelligible) format. Not lateral flow. And the only template we found is for in vitro diagnostics for CLIA approved settings.

We contacted the FDA and we were told to submit a pre-EUA with the proposed testing protocol. Do you have any further guidance to help us expedite this process just so we avoid so many back-and-forths that we present are really solid pre-EUA first and hopefully get through the process quicker?

Timothy Stenzel: Yes. Yes. No, appreciate that and that's why we make this forum available. Again, is it a point of care or in-home?

(Brandon Walker): In-home.

Timothy Stenzel: In-home? So we are working on our recommendations for in-home test development. Would it be by prescription or over-the-counter?

(Brandon Walker): Over-the-counter.

Timothy Stenzel: Okay. So over-the-counter means that health care workers are not involved in selecting and order the test. So that is a higher risk category and our statisticians have been working on study design in that situation and we hope to have specific guidance as soon as possible.

Unfortunately, since that isn't our recommendation as soon as possible - unfortunately, since that isn't finalized, the pre-EUA process is probably the best documented way to go about this to get specific feedback now while we in parallel are working on finalizing the recommendation.

And I depend on our expert staff to inform about what we're going to expect, but just so you know, there may be requirements for a different kind of user testing so that a user understands how to read the device and read whether it's plus or minus and then what's the meaning of that is.

So it goes a little bit beyond the point of care. There's also safety in the home. You know those are the main additional sort of considerations we make.

Also, we expect performance in the accuracy of the test when over-the-counter be extremely well validated and there may be requirements on more than our usual 30 positive and 30 negatives in that situation.

(Brandon Walker): Okay. Understood. Okay. So beyond 30 positive/negative with validated

with PCR we would probably have a requisite number that's higher, you know, 50, 100, whatever it may be.

Tim Stenzel: Right. And our statisticians are working on that based on the calculations and things like that.

Man 1: Okay....

Tim Stenzel: And just to clarify it's in process, and not finalized. So I don't want anything I'm saying here to, you know, be mistaken as, you know, be mistaken for what we are actually require.

So that's why we do invite engagement on the pre-EUA status. And this type of testing, as I mentioned at the beginning is a priority of us. We just want to make sure that especially in a situation where health care workers are not involved, that is, you know, extremely accurate and safe.

Man 1: Got it. And just to clarify, the studies that we're going to propose in a pre-EUA are essentially two-part, one, clinical sensitivity, and two, the usage study as you suggested that we specifically use by lay people. So that's, I'm getting confirmation that that's the route that's appropriate for submitting.

Tim Stenzel: Oh, absolutely. And the flex studies, because if there's any steps that the person's taking in the home, that, you know - if there's any variability involved, time, temperature, volume that you validate for those potential variances and what's the impact on the accuracy of the test.

Man 1: Yes, and apologies. Not to hog the line, this is my last part, but regarding the saliva, we could find - we understand that there are concentrations of LOD guidance, molecular diagnostics for the actual virus per milliliter sample but

we're looking at one of the proteins does the FDA have any guidance on the actual concentrations we should be searching for the proteins per milliliter sample.

Tim Stenzel: Yes, I might look at the direct antigen test because that, I forget how that translates but maybe Toby can help me out , but it's kind of similar to the direct antigen test which look at protein rather than nucleic acid. So it would depend on the copy number of the protein in the virus particle.

So if you're using - if you're targeting a protein that has higher copy numbers than one relative to, you know, the virus particle or in some other ways greatly amplify the virus particle that can - obviously, that would obviously increase your sensitivity, but it also helps your LOD as well.

I just don't remember if the direct antigen test dealt with dilutions of proteins and generalities have to do with...

((Crosstalk))

Tim Stenzel: It may have to do with the whole virus, you know, in terms of dilution series, inactivated, you know, by heat or radiation and/or by a virus. What were you saying , (Toby)?

Toby Lowe: Yes, I was just pulling up the antigen template quickly to look and I don't see anything, but I am looking very quickly. So I would recommend you look as well. Yes, but I don't see it in here.

Tim Stenzel: That's a perfect question to reach out to our template email address and I apologize we could not more directly address your question, but I understand the question and your interest in it and appreciate that.

Coordinator: Thank you. That is all the time we have for questions. I would now turn the conference back over to Ms. Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be made available on the CDRH Learn Web page at www.fda.gov/training/cdrhlearn by Tuesday, June 16th.

If you have additional questions about today's presentation, please email cdrg-eua-templates@fda.hhs.gov. As always, we appreciate your feedback. Following the conclusion of today's presentation please complete a short 13-question survey about your FDA/CDRG Virtual Town Hall experience.

The survey could be found at www.fda.gov/cdrhwebinar immediately following the conclusion of today's live discussion. Again, thank you for participating. This concludes today's discussion.

Coordinator: Thank you. That does conclude today's conference. Thank you again for your participation. You may disconnect at this time.

END