

NWX-FDA OC

Moderator: Monica Pagán Motta
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Coordinator: Thank you for standing by. Today's call is being recorded. If you have any objections, please disconnect now. All participants are in a listen-only mode until the question-and-answer portion 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 conference over to you hose, (Monica). Thank you. You may begin.

(Monica): Good afternoon and thank you for participating in today's call. I'm (Monica Pagán Motta) in FDA's Center for Devices and Radiological Health, CDRH and I'm joined on the call by Dr. Timothy Stenzel, Director of CDRH's Office of Health Technology for In Vitro Diagnostics and Radiological Health, OIR, Dr. Uwe Scherf, Director of the Division of Microbiology Devices in OIR, Dr. (Tamara Feldblyum), Branch Chief of the Viral Respiratory and STI Branch in the Division of Microbiology Devices in OIR, Drs. Yvonne Shea, (Kristy Bialis) and (Anna Mielich), expert reviewers in the Division and Dr. Brittany Goldberg, a medical officer for the Division of Microbiology Devices.

The purpose of today's town hall is to help answer technical questions about the development and validation of the molecular tests for SARS COV2 and the guidance issued Saturday on the policy for diagnostic testing in laboratory

certified to perform high complexity testing under (CLIA) prior to emergency use authorizations for coronavirus disease 2019 during the public health emergency.

Now, I'll turn the call over Tim Stenzel to provide some details on the approach. After that, we'll open the call for your questions.

Dr. Tim Stenzel: Thank you, Monica. I'd like to begin by thanking all of your for joining us today. We appreciate the community of test developers from public health labs to academic labs to commercial labs to kit distributors are working hard to address this public health emergency. Diagnostics are critical to management of emergency emerging viruses. But in the case of this novel coronavirus whether it is spreading quickly, has a long incubation period, and mild undetected cases, the significant role of diagnostics is even more critical.

The American public is depending on us all to ensure that we have access to accurate tests for this virus. We are here to help you in any way that we can.

Today's town hall is intended specifically for test developers. We are here to answer any technical questions you may have about development and validation of tests. Whether you are a lab or kit distributor, we also are here to answer questions about our new policy for labs certified to perform high complexity testing under (CLIA). This policy, which is outlined in guidance dated February 29, enables immediate coronavirus testing by labs certified to perform high complexity testing under (CLIA) if they have completed validation and notified the FDA. The new policy does not change the EUA standard and labs are asked to submit the EUA within 15 days of initiating clinical testing.

We believe this policy strikes the right balance so we can continue to ensure found science prior to clinical testing and follow up with the critical independent check from FDA while quickly expanding testing capabilities in the US. I'm not going to step through every piece of the policy today as this is included in recorded posting of Monday's webinar and I will ensure, and I want to ensure that we have time to answer all of your questions today.

I do want to take a moment to address assay validation. We have outlined validation recommendations in the guidance that we believe are sufficient for a test run in the lab in which it was developed. If a test kit is being distributed, we request that the developer also address shipping, instability testing. The recommended validation for labs and kit distributors is also addressed in our templates that will be posted online.

While these are our recommendations. We recognize that some developers may come up with alternate approaches and we are happy to work with you. Please talk to us early if you're pursuing an alternative approach. We also have seen interest in leveraging CDC's performance data to expedite development and validation of additional assays following the same protocol with the same primer, probes and guides. CDC has granted a right of reference to the performance data contained in CDC's EU A request. and you can refer to FDA Submission Number UA200001, again that's UA200001 to any entity seeking an FDA EUA for COVID-19 diagnostic device.

Therefore the use - therefore developers that use the same protocol, primers, probes and guides may validate their assay with a bridging study. We have received many questions this week on the new policy. Today will post an FAQ, frequently asked question, on our Web site and will continue to update it as appropriate. When questions to our mailbox are not in FDA's purview, we try to facilitate connections with the appropriate parties. To this end, I did

want to take the opportunity to relay an important message from public health partners to labs offering testing under the new policy prior to submission and authorization (in the EUA).

As your notification to FDA is not publicly available until your authorization is complete and posted on our Web site, it would be very useful to state public health departments if you would notify them as early as possible in the process even before receipt of any orders or samples to help ensure they have capacity for validation testing. Those are the five negatives and five positives. And has ancillary information to support case investigations. We also encourage laboratories to be familiar with state and local laws depending - regarding reporting of diseases and conditions of public health significance.

I also want to add that as of this morning, IDT has about 200,000 test reactions on their shelves that are authorized under the CDC and EUA and is ready for sale. You can contact them directly. Again, that's IDT. Please be sure to ask for the CDC authorized kit lot.

I'll stop here and turn to your questions. Thank, you very much.

(Monica): Thank you, Tim. Now we'll begin the question and answer portion of the call. Operator, we'll take the first question.

Coordinator: If you would like to ask a question, please press Star 1, unmute your line, and speak your name and organization clearly when prompted by the automated system. Your name is required to announce your open line. If you would like to withdraw your question, please press Star 2. In the interest of time, please limit to one question. You may rejoin the queue by pressing Star 1. Please unmute your line and speak your name clearly. Stand by. Our first question.

Man: Please unmute if you have a question.

Coordinator: One moment while I gather the name and organization. Our first question comes from (Shaun Young) with DCLA Clinical Microbiology Lab. Your line is open.

(Shaun Young): Oh, hi yes, I have a question. Due to the limited availability of RNA of the virus, are we allowed to use the plasmid as the reference material as well as positive control? Thank you.

Dr. Uwe Scherf: Yes, this is (Uwe). Again, you probably have seen that you might request the RNA from (BI Resources) and currently, we are not aware of other sources that will have the material available. So we request that you go to their Web site and bring up their link to the coronavirus strain as well as the reagents. And then register and lock in and request the 52285.

Man: Our latest information is that they have enough inventory to meet the need and so if you do run into any questions or concerns about the availability of that material, you can reach out to us as well and we'll try to help.

Coordinator: Our next question comes from (Daniel Ortiz). Please state your affiliation, your line is open.

(Daniel Ortiz): Hi, yes, this is (Daniel Ortiz) from Beaumont Health. We had a question about variation from the CDC protocol. If we are using a different instrument for extraction, we are still using the same - we're using a 7500 but it's a 7500 Fast versus DX. Would that require separate EUA approval or does that fall under the CDC protocol and EUA acceptance?

Dr. Uwe Scherf: So you will need to have something like a bridging study performed in order to demonstrate that the data that are generated are equivalent and after doing so, you will need to submit an EUA to the agency.

(Daniel Ortiz): Thank you.

Man: If you're an LET developer that's notification that you've completed that. And then you can begin testing and then you have 15 days to submit your bridging study information.

Coordinator: Our next question comes from (Badia Dacal). Your line is open.

(Badia Decal): Thank you for taking my question. My question is you described bridging studies, but can you clarify a little bit on types of bridging study using just the EUA kit on label as described on the package and serve versus the bridging study you described on the previous caller's answer? Thank you.

Dr. Uwe Scherf: Well if you have a completely different protocol of changing the steps is your protocol, then you will need to perform an MU evaluation on the LOD side and with the clinical samples. So I think there are nuances there that you need to be aware of. I think bridging studies are for very small changes that can be done. What I'm hearing from you now, you will have an in-protocol. So there you will need to generate the data in order to validate your assay as described in the guidance document.

Woman: (Unintelligible) issuing further guidance regarding bridging studies in the future. We will posting more information shortly.

Man: In the meantime, do send us an email to the template email address if you have questions about bridging studies before that's posted.

Coordinator: Our next question comes from (Muhammed). Please state your affiliation. Your line is open. If you could check the mute function on your phone, (Muhammed), your line is open. Please state your affiliation.

(Muhammed): (Muhammed) (unintelligible). I believe my question was answered. I was asking how we can obtain positive control. But if you can explain more about that, that would be great. Thank you.

Dr. Uwe Scherf: So the positive control that is needed for your - needed for the IDT can be obtained from CDC as part of their assay. So you might want to reach out to CDC to obtain some of that material for your evaluation.

Man: And if you would want to develop that on your own, those are both transcribed (unintelligible) both for the N1, N2 and N3. As well as for the RP. So, that could be developed on your own. I would just check on with us at the email address to see many details about how you would do that.

(Muhammed): Okay, thank you.

Coordinator: Our next question comes from (Clint) (unintelligible), please state your affiliation. Your line is open.

(Clint): Hi, I'm affiliated with Qua Telehealth and Wellness, a telehealth company. My question is along the lines of rapid antibody testing. Does the FDA see any guidance or template develop for an EUA for rapid antibody testing in the future?

Dr. Uwe Scherf: Yes, we do, however, if you already have ideas and have validation approaches that you believe are solid, we encourage you to share that with us

in order to expedite the review process on that end. We are developing a template as well. But again, if you already have approaches courage you to share that.

(Clint): Through the same email as the present template email?

Woman: Yes, you can use the same email and also you can provide specific questions (unintelligible).

(Clint): We've received some kits already that we've just been testing, but obviously we can't use these until that process I approved.

Man: Can you explain in a little more detail of what you have?

(Clint): These are just, you know, open-source, available rapid antibody tests through China sources. And it gives you, you know, it's the two membrane layers and gives you the antigen antibody and an anti-antibody for a rapid antibody detection.

Man: Is it allergy-based or-

((Crosstalk))

(Clint): IGM-IGG.

Man: Okay, yes, I think it's best to reach out through the email to find out what you may need to do about that issue.

(Clint): Yes, I reached out initially and they told me it wasn't being considered at this time.

Man: We will revisit that. If you could send an email again, I'll ask the team to address that question now. Also we'd like to know the manufacturer so that we can reach out and work with them on an EUA.

(Clint): I will write all that information for you. Obviously, we really, a very important issue for using it like flu as a positive result matter. The negative result doesn't necessarily matter as much.

Man: Okay.

(Clint): Appreciate it.

Coordinator: Our next question comes from (Jason Park) with Children's Health, Dallas. Your line is open.

(Jason Park): Thank you. I had a quick question under the CDC kit EUA. Are we allowed to drop the N3 primer probe set and just run N1 and N2?

Man: If you're using the CDC design, yes. There EUA authorization is in the process of being updated, but we've already given that authorization to them.

(Jason Park): So we do not have to run primer and probe for N3?

Man: That is correct. And I would, thank you.

Coordinator: Our next question comes from (Arian Lindsay) with (Milan) Pharmaceuticals. Your line is now open. (Arian Lindsay)?

(Arian Lindsay): What happens after the EUA isn't a novel predicate, would these tests be taken off the market then and have to go through the normal route? Or what will happen afterwards?

Man: So, you know, under the EUA laws and regulations, that is a possibility. That's way too early to speak, about right now. Previous emergency authorizations, we have begun going through that process such as for Zika and for Ebola. We're in no rush though to remove available tests from the market following introduction of full (unintelligible).

(Adrian Lindsay): Okay, thank you.

Coordinator: Our next question comes from (Jan Nak) with Roswell Park Cancer Institute. Your line is open.

Dr. Tim Stenzel Thank you. This is Dr. Stenzel, I just want to thank you for your hard work on this. I think my question has already been answered, but I just want to highlight the importance of this. This has to do with using an instrument other than the 7500 DZ for the detection part of either the CDC assay or New York State's EUA assay. As it would be very useful if you could delineate what is necessary to accomplish these bridging studies.

As it, and up until a few seconds ago, I thought the only option was to do a complete validation of this assay which is a big lift. If we could just somehow accommodate that change in instrumentation. I've got - there are many labs that have a 7900 or other instruments other than 7500 DZ that could be bringing up these assays very quickly, but they're unable to do that because of the requirements for a 7500 DZ. So that's my comment. So thank you.

Man: You're welcome and thanks for the kinds words. Yes, we want to make this as easy as possible. So if it is the CDC design, a bridging study, we believe is going to be sufficient. If it demonstrates similar performance as outlines in the original CDC EUA authorization which is available online as far as those things like LOD. So if you have a proposal that you'd like to submit to us for review on how you might do that bridging study, and you identify the instrumentation you want to bridge too, you can send that to us at the template address. And we will review it and comment on it.

Coordinator: Our next question comes from (Cassandra Fisher). Your line is now open.

(Cassandra Fisher): Hi, I'm from (unintelligible) Scientific. I just wanted to know if there's another way that we can test for this virus besides using assays, for example would CAT scans, would that provide any type of accurate results?

B: Hi, this is Dr. (Goldberg). That's a very good question. Right now we're still kind of worrying more about this virus. I've not yet heard anything describing CAT scan be used to differentiate between COVID and other respiratory tract infections. However, we're still learning more about this. And we will see what happens as more information becomes available.

(Cassandra Fisher): Thank you.

Coordinator: Our next question comes from (Nicholas Stanford) with Microgen Diagnostics. Your line is open. (Nicholas Stanford), your line is open. Our next question comes from (Neil Lindeman). Your line is now open.

(Neil Lindeman): So first thank you very much, Dr. Stenzel and your colleagues for helping guide us all in developing these assays. My question is maybe just to confirm an assumption that I have which is we have all the elements needed for the

EUA assay, but we probably won't be able to scale for our entire patient volume. And so we may end up having to bridge to a higher throughput assay. And my question is whether or not we can bridge to our own deployment of the EUA assay or do we have to do a bridging study with a different lab?

Dr. Uwe Scherf: No, so if you have initially validated your assay and you are certainly our throughput setting and then you are moving forward to a larger setting, the bridging study can be done in-house with basically you can tell us in between the different capacities that you have available. There will not be any need for going outside of your organization.

(Neil Lindeman): Thank you so much.

Coordinator: Our next question comes from (Marcela Prado). Your line is open. Please state your affiliation.

(Marcelo Prado): Yes, thank you, (Marcelo Prado) from UC Davis Health and I had a question regarding the CDC EUA assay and specifically the human specimen control. Is there a specific lot side to the CDC EUA authorization? If not can we order this control through IDT directly if we're unable to acquire it through CDC purchasing? And when looking at this control through IDT directly, it appears to be a different suspension buffer as well as PH. So is this control acceptable using the EUA or will this render it an LTD?

Dr. Uwe Scherf: You made a good point there. There are slight differences. So the use of the CDC material is clearly preferred.

(Marcelo Prado): So if we are unable to acquire it through CDC and we use the variance, if you will, will we then be required to perform the LTD validation if used with CDC primer probed and positive control reagents?

Dr. Uwe Scherf: We think that a small bridging study to the CDC reagent will suffice for this.

(Marcela Prado): Could you please provide some clarification regarding that bridging study that would be required for this extraction control?

Man: No, you know, if you wanted to propose a plan to us that you think would be sufficient for your lab and send that to the template email address, we will respond as quickly as possible. We have a team that is looking at these. We've taken notes down, so we will attempt to put additional information as when we talk about various options for bridging studies and we will include this as well when we post that.

(Marcelo Prado): Okay, thank you very much, and thank you for taking my question.

Man: You're welcome.

Coordinator: Our next question comes from (Sarah Young), your line is open. Please state your affiliation.

(Sarah Young): Hi, yes, thank you. This is (Sarah Young) from Children's Hospital Colorado. I'm asking a question that is somewhat similar to what others have been asking already. This is having to do with extraction kits particularly the extraction kit that is associated with the CDC assay. So we have tried to order extra extraction kits, but they are on backorder as is every other material for the CDC assay. So I guess what I'm asking is would we have to do a bridge study and then submit for an EUA just because we had to order different extraction kits for other respiratory assays that we run. Just because there's a big backorder. Thank you.

Man: Tim, do you want to take that?

Dr. Uwe Scherf: Yes, I think what you are describing now is that there will be a validation needed from your perspective that you are completely using a different extraction method. So the LOD and clinical evaluation is something that needs to be provided in order to assure proper performance. So that will be that you will need to submit an EUA in this setting.

Woman: Dr. (Young), so I completely agree with my colleague, Dr. Scherf. So just to clarify, you may use an extraction kit within side your lab. However when you do so, please go ahead and notify FDA once you complete validation. At that time, you may begin testing patient samples. When you are complete with - you fill out the accelerate EUA template and incident that's FDA.

(Sarah Young): Thank you. I guess I just sort of worry about backorders on a lot of these, I guess you could say, ingredients for the assay because we've tried ordering them and I guess I just hope that manufacturers will be able to scale up in the coming time. Just because right now it's really difficult to obtain these reagents within a timely manner.

Woman: I understand and if you have anything that you can assist us with, please feel free to notify our email address and we'll do what we can to connect you to any resources we have available.

(Sarah Young): Okay, thank you so much.

Coordinator: Our next question comes from (Mary Jacobsen) with (Alpha Medical). Your line is open.

(Mary Jacobsen): Thank you. I would like an update on feasibility of self-nasal swab collection testing. Specifically to eliminate the need for sick patients to have to do in-person care. And I'm from a telemedicine company.

Man: Hi, so with regards to an update, I'm not sure that we have anything from FDA to report. However, I emphasize that FDA is really interested in working with people that develop new test kits and new technologies including (unintelligible) patient testing. So if you do have any proposals for any of your patient, you know, test kit, please feel free to reach to us at the EUA template mailbox and we're happy to discuss it with you.

Man: We've been working with some developers who have proven say for influenza that (unintelligible) nasal swab is something that is acceptable. So we're going to be very open to this. And work closely with you to make this possible.

(Mary Jacobsen): Thank you.

Coordinator: Our next question comes from (Liz Thomas) with ACLA. Your line is now open.

(Liz Thomas): Thank you. This is (Liz Thomas) with the American Clinical Laboratory Association. I've got a quick question. Many of our members who are at large national, commercial laboratories have been working closely with the CDC who have told us that in order to receive the CDC kit, we need to go through a material transfer agreement with the CDC. However, earlier on this call, I think it was mentioned that commercial labs that want to receive the CDC kit should purchase the kit directly from IDT. So I just wanted to clarify that.

Man: Yes, that's absolutely true. We're, the CDC is working closely with a number of manufacturers to make tests available through other channels other than

directly from the CDC. IDT is one that we can publicly announce today. We expect to make, you know, an announcement in the next couple of days that we'll - QC testing is successful with another provider. So but for right now, IDT is shipping to labs across the US and they do have inventory on their shelf. It is, at least as of this morning.

(Liz Thomas): Okay, thank you so commercial labs that want to receive the CDC kits to begin testing should go through IDT or should we continue to work with CDC?

Man: It depends on your need. I mean if you - if there's any delays getting anything through the CDC, you have the option of going directly to IDT when we have material available. And there's also a new lot received at the CDT today from IDT. So hopefully that has it's QT and additional material will be available. So it's your choice. And we're just trying to make as many options available in the market that we can.

(Liz Thomas): Thank you.

Coordinator: Our next question comes from (Inca Wachaski) with Akron Children's Hospital. Your line is open.

(Inca Wachaski): Yes, I just had a question regarding why the CDC decided to go with the N gene while, for example, the WHO decided to go with other gene targets and other kind of (unintelligible) using other targets.

Man: Sure, we are working with developers around the world to bring on additional manufacture kits that are of different design. And certainly an (LAK) provider that wants to develop their own task base, based on an alternate design that you read about. You have that pathway through the guidance policy. The

guidance policy that we issued last Saturday. But, you know, stay tuned as far as additional manufacturers. As to why the CDC chose just the N gene, I would direct those questions to the CDC. I'll just say that our review of their EUA package was excellent. We had no issues with the design. They did target two different (unintelligible) of the N gene. So a three different targets, two are specific for the novel and then one was for a more pan SARS region.

(Inca Wachaski): Thank you very much.

Coordinator: Our next question comes from (Dwight Oliver) with UT Southwestern Medical Center. Your line is open.

(Dwight Oliver): Hello, thank you for taking my call. This is (Dwight Oliver) from UT Southwestern. We're developing a lab-developed assay and my question was under the guidance it says for the limited detection testing and for the contrived positive specimens you can spike with the virus or with RNA. So I wasn't sure if that had to be whole viral RNA genome or it could just be our target RNA.

Woman: We prefer to have whole virus. It represents better the organization and therefore whole virus is preferred especially now that it is available. You can try to obtain it from DI as was mentioned before. You can also use an activated virus if you can find that or you can even use patient samples and isolate the RNA (unintelligible) patient samples.

Man: I think the easiest approach is to place an order with BEI. They assured us that RNA is available, activated RNA is available. And I know they're also working on inactivated virus, but there's no need to wait for that.

(Dwight Oliver): But if there's a delay in getting this from BEI, if, you know, the material transfer agreement and all that is delayed, will you still accept spiked small RNA fragments?

Man: What I would suggest if that if you have an alternate plan that you outline that for us and send it to the EUA template address and we will respond. It would be preferable though if you could obtain the whole virus and (unintelligible) have worked hard to make this kind of material available in order to assure everyone that the performance of this test is adequate to meet this emergency.

(Dwight Oliver): Okay, thank you very much.

Coordinator: Next we have (Didi Peterson) with (Genomic Expressions). Your line is now open.

(Didi Peterson): Hi, first of all thank you so much for providing this guidance. My question is more in line with the lady from the telecommunication company or telehealth company. As I think that the more testing we can get done in a local setting the less spread we will have. And having looked at a lot of different options for systems where the patients can self-collect and specifically interested guidance on how they will go about that for the EUA and validation.

Man: So what kit will you be using for Number 1 for your laboratory test? Will you be using a CDC authorized kit or something from another provider?

(Didi Peterson): Yes, so if we can get our hands on the CDC kit, that sounds like the easiest solution.

Man: All right, I think it's a relative straightforward matter. Obtain what type of samples that you're intending to use with that, that might differ from others

and it would be helpful, I think, to have actually lay users demonstrate that they can do this. And that if they are going to shipping it, let me do the shipping study so that you can demonstrate that there are no issues related to shipment because most of these patients will not be positive, you can spike those samples with viral RNA in order to, you know, match the metrics that you intend to validate.

And I'll turn it over to some of my colleagues here if I misspoke. If they want to add anything.

Woman: Usually what you request is when you try to add a new specimen type is to have a comparison study between the approved or in this case authorized specimen type versus the new one. And so as Dr. Stenzel mentioned that would be an appropriate study to compare self-collected to what would be collected by healthcare provider and a shipping study as well.

Dr. Tim Stenzel: Yes, and it all can be done at your site with self-collection on site. You package it. You ship it back to yourself. And then do the comparison testing.

(Didi Peterson): Okay, that was very helpful. You mentioned that there was a kit (unintelligible) approved. Could you provide information on that?

Dr. Tim Stenzel: I'm sorry. Could you repeat the question?

(Didi Peterson): You mentioned there was a collection kit approved for influenza for self-collection.

Dr. Tim Stenzel: No, it's-

(Didi Peterson): No? Okay.

Dr. Tim Stenzel: I'm sorry. Does somebody want to answer that question?

(Didi Peterson): I must have misheard because I thought there was a collection kit approved for collection of influenzas.

Dr. Tim Stenzel: We just went on mute just for a second. So yes, I apologize for any misunderstanding. We know that there's been research that's been performed with flu self-collection. It's under OID authorized collection protocol. We know that it was - we do know it was also that study even within that publicly known that it is effective for flu. So there's no FDA authorized self-collection for flu that can be immediately used. However, this - we believe this is simple and straightforward design of a study to show equivalency between what's CDC (unintelligible) and self-collected sample that's undergone a simple shipping test.

(Didi Peterson): Thank you.

Man: I would also like to iterate that we know there have been some delays in getting BEI viral RNA, affected RNA, but as of yesterday, we were told that backlog cleared and that within 72 hours of order, you will get that virus. So they have stated that going forward, they don't believe that they'll have an inventory problem supporting the needs for the test development community. So just please reach out to them and place your order as soon as possible.

Coordinator: Our next question comes from (Omar Green). Please state your affiliation. Your line has been opened.

(Omar Green): (Unintelligible). So (unintelligible) or is there another mechanism (unintelligible)?

Woman: Could you please repeat your question? We had a little trouble hearing you. If you could please repeat your question.

Dr. Tim Stenzel: You may be on speakerphone. It might be good to pick up the handset because we just had difficulty hearing the question.

(Omar Green): This better?

Dr. Tim Stenzel: Much better.

(Omar Green): Okay, so the question is if we are not using a PCR DNA-based approach does that necessitate an LDT approach?

Man: If you're not using a PCR what approach?

(Omar Green): If we're not using a DNA-based approach, we targeting something other than DNA. Does that necessitate an LDT approach?

Woman: So you're referring to like a serology test or an antibody antigen test?

(Omar Green): Yes, in that general category.

Woman: Sure, yes at this time, we still consider an EUA for that purpose. Please go ahead and reach out to the email address and document what it is you'd like to do and what your validation protocol will be.

(Omar Green): Okay, so just reach out to the email. Okay, all right, thank you.

Coordinator: Our next-

(Monica): Operator, we'll take the next question.

Coordinator: The next question comes from (Joel Lefforts). Please state your affiliation.
Your line is now open.

(Joel Lefforts): Thank you. This is (Joel Lefforts) from Hitchcock Medical Center. So we have a question regarding using RNA to create the contrived sample for the validation studies of an LDT (unintelligible). We're a little unsure if it would be acceptable to spike in the RNA either before or after if those options would be okay for spiking it before or after doing the RNA extraction when we're spiking into a negative patient sample. We're a little concerned. Ideally, you would spike it before, but we're concerned about the RNA degrading in that raw patient's specimen.

Dr. Tim Stenzel: Are you talking about spiking, I just want to clarify, spiking extracted viral RNA or (unintelligible)?

(Joel Lefforts): Yes, extracted using an EEI genomic RNA-

((Crosstalk))

Dr. Uwe Scherf: This is Uwe. We understand your challenge. What is needed clearly is that the RNA needs to go through the extraction process of your test rule. We recommend that you work on stabilizing strategies that you utilize in order to avoid degradation of the RNA when you spike it in the sample. What people have used is having the license (unintelligible) already in the sample and then you, at the later stage, add your appropriate amount of nucleic acid, the RNA and then immediately move onto the extraction.

But from your, kind of, (unintelligible) perspective, it's important that you take the nucleic acid through the extraction process in order to mimic an appropriate contrived clinical sample.

(Joel Lefforts) That's really helpful. Thank you. Would you have the same recommendation for both the LOD and the, all the other spiked in accuracy samples?

Dr. Uwe Scherf: Yes, we have. If you send your request to the email then we will share with you the approaches that we've seen have been acceptable and has been successful.

(Joel Lefforts): Great, thank you very much.

Coordinator: Our next question comes from (Russell Garlic) with LGC (Fair Care). Your line is now open.

(Russel Garlic): Thank you very much. Great discussion, so we have prepared already a high side of stock of the (COS CP2), by taking 27% of the genome and (unintelligible) it up into (Symbus) with the recombinant technology. (Symbus) is an RNA virus. And so it has all the sequences for all these assays we've talked about.

And it's, right now, at a high tide of stocks. So it's being used by IBD manufacturers for their kits. My question is the performance we're seeing in the clinic with viral transport medium would like to design a low positive control that is reflective of the samples you're getting (unintelligible) laboratories with their LODs. So my question is, what types of levels are we seeing? Can you give us some guidance on what would be a good low-positive control for determining sensitivity? Thank you.

Woman: Usually positive control is about 2 to 3X LOD with the assays. Those you have a sample that's very weak, low titer or your positive control can still detect that. That's the average, but certainly you can - you may need to test what works with your assay.

Dr. Tim Stenzel: Yes, so the LOD would be established with your (unintelligible). They just among those that looked at the CDC assay. We are able to detect down to 2 to 5 viral copies with their assay. But that just gives you 2X to 3X LOD above that.

(Russell Garlic): Great, in the clinic, are you seeing a lot of samples at those levels?

Dr. Tim Stenzel: No, I do have some knowledge. It's incomplete. Obviously we're still early, but there can be some very low viral (unintelligible) viral copy number in clinical samples. So it's important to know your LOD and to establish that and for the assay to be as sensitive as possible.

(Russell Garlic): Yes, so last comment, we're working really fast to get it available to all these laboratories who need this material for assay validation. So just check out our Web site. Thanks, everybody.

Dr. Tim Stenzel: Okay, and I would say that labs are doing their own development can, you know, go ahead and purchase that one that's available. If they're doing their own an ways and validate it for their purposes. Also if you would like to have your material be reviewed, basically performance by us. You know, just go ahead and let us know through the template email. And we'll work with you and perhaps can establish some sort of, you know, (unintelligible) CDC assay and it might be useful to other (unintelligible).

(Russell Garlic): Okay, thank you.

Coordinator: Our next question comes from (Paul Leopard) with Michigan Medicine Microbiology Lab. Your line is open.

(Paul Leopard): Hi, (Paul Leopard) here, a quick practical question. Are kit manufacturers that are providing RUO kits or availability of RUO kits, are individual labs allowed to receive those and perform then the EUA evaluation according to the template?

Dr. Tim Stenzel: The way that the new policy reads is that RUO components can be used to build (NLBT). So it was not intended for it to be a complete kit. And so, those manufacturers with the complete kit which will include all primers and probes and controls, instructions for use should come directly to us for EUA authorization, through the kit manufacturer route. However, you know, again, (LET) developers can purchase components from such companies that are RUO labeled and create their own (LET) and validate it and notify us. And they can begin testing.

(Paul Leopard): Okay, thank you.

Coordinator: Our next question comes from (Sarah Harlahade) with the University of Pennsylvania. Your line is now open.

(Sarah Harlahade): Hi, I actually have two questions. One, the first kind of relates to the last question. If we are developing something by a manufacturer who has submitted for EUA and they've submitted their (infilago) analysis, can we use that by proxy for our - if we're submitting an EUA to bridge the gap between their approval and our use in our lab? And then my second question is, or do you want to answer that one first and then I'll ask my second?

Dr. Tim Stenzel: You know, so the way that our process normally works is that if a company is willing to give you a right of reference, such as the CDC has now provided for any developer to be able to reference their EUA package and all the data that they accumulated with their design in support of an (LBT) developer using primer and probes and wanting to piggyback on that and just doing a relatively straightforward bridging study. So if another (IBD) developer has given you a right of reference then that is all legal and we can use that in your - in the view of the application.

(Sarah Harlahade): Great, thank you. And then my second question if there is guidance on once you have your assay up and running to send your first five positive and five negatives for confirmatory testing, what is the guidance if our limit of detection is not as sensitive as the assay where we may be getting negative, that would be positive on the CDC assay.

Dr. Tim Stenzel: Yeah, so do you know that your (LOD) is going to be not as sensitive as the CDC's assay? Or is that a potential problem?

(Sarah Harlahade): I don't know that yet, but I'm just - we're project that I may not be that sensitive to the same level the three to five copies.

Dr. Tim Stenzel: I think that's a perfect question once you know your (LOD), and you are concerned about that. And I would say that most clinical samples even though they're going to be, some of them are at a high CT. Probably well above the limited detection of the CDC assay. So it would have to be an (LOD) that was significantly different from the CDC's in order to make any clinically meaningful impact on the testing.

Woman: And I'd just like to remind everybody that per guidance, if you are not getting your first five positives, please just go ahead and reach and notify FDA and

we'll work with you to determine what else needs to be done if anything for your assay.

(Sarah Harlahade): Thank you.

Dr. Tim Stenzel: A lot of listeners on this call know that the new templates and frequently asked questions are now up on the FDA Web site. So, you know, we look forward to those being useful to you. Operator, we'll take our last question.

Dr. Tim Stenzel: Our last question comes from (Mike Mahala) with ACL Laboratories. Your line is open.

(Mike Mahala): Good morning or good afternoon. So my question has to do with instrumentation. We propose to perform the CDC vetted (unintelligible) methods but my question is can we use the ABI 7500 RUO instrument and just update the software so that it's identical to the 7500 DX?

Woman: You can do so if you validate it in your lab. I understand that this is going to be used only in your laboratory, is that correct?

(Mike Mahala): Correct.

Woman: Yes, for your laboratory, you can validate the test on the ABI 7500 with the updated software. The easiest way would be to compare with another ABI 7500 (unintelligible) to show the equivalence if you don't have access to that, then you would just go through validation that's required in your laboratory and that would be acceptable.

(Mike Mahala): Right, so you would do - we would have to do the LDT?

Woman: Yes.

(Mike Mahala): So we wanted to not have to do that obviously. So there's no way to just perform the validation with the updated instrument software? You'd still have to do the full LDT?

Woman: I suggest that you send your question through this template mailbox. We will consider that, from what I understand right now it seems like you would still have to do the validation.

(Mike Mahala): Okay, thank you very much.

(Monica): Thank you, operator. We'll go ahead and make some concluding remarks. A slide presentation about the immediately in effect guidance is available on CDRH Learn at www.fda.gov/training/cdhrlearn under heading Special Technical Topics, subheading in vitro diagnostics. And the transcript for that webinar will be available shortly today as well.

Again, templates for EUA submissions by laboratories and manufacturers as well as frequently asked questions on the diagnostic testing for SARS COV2 are now available on CDRH's emergency use authorization webpage. If you need additional information completing this EUA template, would like to know how to submit your pre-EUA submission to FDA or wish to consider using an alternative specimen type, please contact the Division of Microbiology devices at 301-248-1778 or email CDRH-EUA-templates at [FDA.hhs.gov](mailto:CDRH-EUA-templates@FDA.hhs.gov).

Thank you, everyone, for your participation in this call, and this concludes today's call.

Coordinator: Thank you for your participation. You may disconnect at this time.

END