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

**Moderator: Irene Aihie
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12:15 pm ET**

Coordinator: Good afternoon and thank you all for standing by. For the duration of today's conference, all participant's lines are on a listen-only mode until the question and answer session. At that time if you would like to ask a question press star 1.

Today's call is being recorded. If you have any objections you may disconnect at this time. It is my pleasure to introduce Ms. Irene Aihie. Thank you, ma'am. You may begin.

Irene Aihie: Thank you. Hello. I am Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 19th in a series of virtual town hall meetings to help answer technical questions about the development and validation of tests for SARS-Co-V-2 during the public health emergency.

Today Timothy Stenzel, Director of the Office of In Vitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality, and Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and

Radiological Health, both from CDRH, will provide a brief update.

Following opening remarks, we will open the 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 Toby.

Toby Lowe: Thanks, Irene. Thanks, everyone for joining us on these town halls. I have a couple of updates. As we've discussed previously, we are - we've been working on updating some of our EUA templates that are available for you all to help facilitate your EUA submissions.

And yesterday we updated the Molecular Diagnostic templates, both for commercial manufacturers and laboratories to include additional information on our recommendations for validation of pooling strategies. As well as, multi-analyte respiratory panels. And in the manufacturer template, also included recommendations for point-of-care testing.

Along with those template updates yesterday, we updated the FAQs. So we updated the question on the FAQ page related to pooling. And we added questions related to point-of-care and multi-analyte respiratory panels.

And then just before this call we finally got out the much anticipated, formerly known as, at-home test. Now known as non-laboratory use test template for manufacturers of molecular and antigen diagnostic tests. So that was just posted about 20 minutes ago, along with an update to the FAQ about those types of non-laboratory or at-home tests. And with that, I will turn it over to Tim.

Timothy Stenzel: Thank you, Toby, and welcome everybody. We look forward to these conversations and assisting in any way that we can.

A couple of updates. One is on LabCorp. Many, if not most of you, have seen that we have authorized LabCorp for both pooling and an asymptomatic claim. So this is the first authorization where the FDA has authorized a test developer to claim performance in the asymptomatic population. And we welcome additional, both pooling and asymptomatic submissions.

I want to just briefly review pooling, and just make sure that everybody on the call today knows that we welcome pooling. With the template updates, we've provided even more information on pooling that find, we hope, to be helpful. Nothing really has changed in what our recommendations are for validation. But I do want to clarify the regulatory pathway for pooling.

As we have seen highly variable results, even on the same platforms in different labs. We believe that the science here is still evolving. And we would like to be involved in the pooling. However, we've made it very regulatory friendly. That is, go ahead and validate your pool. We ask that you follow the recommendations if not, and contact us.

But once you've validated the pooling, and if you follow our recommendations, you don't even, you know, need to have contact with us. Validate it. Once you validate it you can start pooling while you work on pulling the data together and submit it to us within 15 business days.

We would ask that you notify us, as well, when you begin that pooling testing, and that you've finished validation, so we can be on the lookout for your data when it comes in. And then after you submit, and during that whole time, you can continue to test. As long as you don't experience any issues.

And we'll receive it. I'll take a quick look at it. We'll assign it to a staff member.

If we have any concerns we'll reach out. But all during this time, unless you hear from us, you can continue to test. So this is a bit on the honor system as we say, that the labs will do a good job validating this. And manufacturers, as well. And we look forward to working with you to expand testing in this way.

And then one last update is that you may have seen yesterday, an amendment update for Quest testing - their LDT testing. They submitted a new extraction method that gives them greater throughput. Normally we don't make these updates that big a deal, although they're all important to all the developers. But the new update allows Quest to test 36,000 - that's 36K or 36,000 more tests - up to, more tests per day.

And then if you add pooling on top of that, which they're already authorized to do pooling, then they can substantially increase the throughput.

And we welcome working with all developers, including kits and labs, to help you know, provide more testing. And most of these pathways don't require an EUA authorization to get started. The new non-laboratory testing template that was just posted for molecular testing and direct antigen testing outside of a healthcare facility, will add additional testing as well. And then of course the non-laboratory collection also adds.

So these are all the things that we are trying to do to help facilitate and to see implemented, additional testing across the country.

And with that, we can turn this over to questions. And hopefully, we can give you some good answers. Thank you.

Coordinator: Thank you. If you would like to ask a question, please unmute your phone, press star 1, and record your first and last name clearly when prompted so we

may introduce you. Again, that is star 1 to ask a question. Our first question comes from Shannon Clark. You may go ahead.

Shannon Clark: Hi, this is Shannon Clark with UserWise Consulting.com. I just had a question to follow-up. Dr. Stenzel had noted in multiple, previous town halls that the threshold for sensitivity for IgM is 70% for serological test kits. And from what I understand, that's subject tested two weeks after symptom onset. Not necessarily when they got tested with PCR.

So I was just wondering if there's a minimum sample size for IgM results? Can we test five individuals and get 100% sensitivity? Or is the minimum sample size for IgM results 30 subjects?

Timothy Stenzel: Yes, that's a great question. Happy to clarify. Yes, it's a minimum of 30 positives per isotype. If all the samples are positive for both IgM and IgG, obviously all you need is 30 samples. But if there's not complete alignment between IgE and IgM, for example, then you may need to go above that 30.

But as IgM is coming up just about the same time as IgG comes up, in most of these patients, hopefully, that's roughly about 30 samples. Thirty positive samples total. Hopefully, that addresses your question.

Shannon Clark: And is that 30 positive and 30 negative, or 15 positive and 15 negative?

Timothy Stenzel: For serology it's 30 positive. And then a minimum of - Toby correct me, of 75 negative. But it also depends on the cross-reactivity testing that you do. There are different formulas there, depending on how you do your negatives.

Many developers are doing a whole lot more negatives so that they have a better estimate. And we have - it's not a requirement, but they do it to have a better

estimate of what their negative percent agreement, is. And so we know what - in general, what the specificity is so that we can, you know, we know what positive predictive values will be. And negative predictive values will be for these serology tests.

Shannon Clark: And in point-of-care testing is it necessary to simulate sample collection in the case of - use of a lancet? Or can we use leftover samples that were previously collected, and use those as part of point-of-care testing?

Timothy Stenzel: What kind of leftover samples do you have?

Shannon Clark: So there were samples collected by finger stick and kept perhaps, in a vial, could we use those as part of our point-of-care testing? Or is it important to have a live patient there, and simulate - not simulate, but run through finger prick as part of the point-of-use testing?

Timothy Stenzel: Yes, we're open to that. I'm not familiar with how you would stabilize the finger prick sample for very long. And so I think that kind of detail would require a little bit of dialogue with our expert review staff on how to make sure that that's going to work well for you.

Shannon Clark: Excellent. Thanks so much.

Timothy Stenzel: For those who might have a similar question, we do view venipuncture and finger prick as different sample types. And then because they are not physiologically the same, with the venipuncture you have good mixing of all components in the blood. In a finger stick, you can have alteration of that. All right? Thank you.

Toby Lowe: And I think to add on to that, if your samples that you're using were not

collected in the manner in which you intend to collect them for use of your test, we would need to discuss that with you. And consider, you know, whether you have any data to demonstrate that - the difference in collection methods does not change your results.

Shannon Clark: Perfect.

Timothy Stenzel: Yes, good point Toby. And, to make sure that you don't carry that way of collecting and storing into your authorization. Because we can only authorize, what we have data to authorize. All right, I think it's time to probably move on to the next caller.

Coordinator: Our next caller is (Andrew Waliliae). You may go ahead.

(Andrew Waliliae): Hi, thank you. Hi Tim and Toby. Good to talk to you again. I have a quick question around collection devices. The particular one I'm talking about today is a saliva collection device. But I guess it's a similar question for collection devices in general.

So my understanding, and correct me if I'm wrong, is that a collection device would not apply for an EUA by itself. But rather apply with a test maker or a CLIA lab. But if the maker of the collection device is themselves a CLIA lab, who are using a test that already has a EUA authorization, could they potentially use that test, together with their collection device, to do a new application? And then use that application for their letter of reference to other manufacturers - or other CLIA labs rather, that they may want to sell their collection device to?

Timothy Stenzel: Toby, do you want to - you've been kind of focusing a little bit on that.

Toby Lowe: Sure.

Timothy Stenzel: Do you want to respond?

Toby Lowe: Yes, so I'm not sure I followed all of the pieces there, but let me, you know, start from you know, sort of the basics with collection devices.

So collection devices we do consider to be devices. And we do review them, you know, generally both before and during the pandemic, as standalone devices.

During the public health emergency, specifically for saliva collection devices, we do want to ensure that they have been appropriately validated. And we can do that in a couple of ways. We have authorized tests that include specific collection devices. And so in those cases the collection device is considered part of the test system and is authorized as such.

That does not mean that those collection devices have an authorization. They are only authorized within that EUA as a system.

Collection devices can also submit their own EUA to get their own authorization, similar to how we've authorized a couple of standalone home collection kits. We can do that both for home collection and not. Such that the collection device itself would have an authorization. And then other tests can leverage that authorization and incorporate it into their EUA. So a test could request in their EUA, to be authorized for use with that previously authorized collection device.

(Andrew Waliliae): Got it. So they could just use their EUA authorized test that doesn't have a collection device, with their collection device for the holistic validation?

Toby Lowe: Right. So right now a lot of tests are authorized, you know, with sort of what we would consider, standard respiratory specimens. Like NP swabs and nasal swabs. And those swabs also are devices that have regulatory requirements for them. Most of them are 510(k) exempt, meaning that we don't need to review them.

We would just expect them to follow, you know, the other regulatory requirements like registration and listing and adverse event reporting and whatnot. But we wouldn't need to see a submission for them.

And then other collection devices like saliva collection devices, do generally require pre-market review. And so during the emergency, we are considering EUAs for them.

(Andrew Waliliae): Great. Okay, great. Thank you so much.

Toby Lowe: Sure.

Coordinator: And before we go to the next question, as a reminder, if you would like to ask a question press star 1. We are taking one question per caller. Our next caller is Jason Robotham. You may go ahead.

Jason Robotham: Hi. I've seen an increased number of antibody tests being advertised and administered by doctor's offices, chiropractors, allergists, etcetera. And they're being offered as finger-prick tests.

So this raises a lot of questions. But I guess the simplest is whether or not there's any way manufacturers or distributors are actually allowed to sell their tests. Whether they have EUA or have just provided notification to these types of

places, given that they're not likely to be CLIA certified. And to my knowledge, no test has been authorized for use via finger prick.

Timothy Stenzel: Thanks, Jason. Yes, we have not - unfortunately, we have not yet had a complete package that we could - until - and maybe there's something inhouse now. But we haven't had a complete package to - giving authorization to a point-of-care, CLIA-waived - deemed CLIA-waived serology test.

We're very open to it. We just ask the developers, you know, follow our recommendations or they're going to want to do something else to connect with us. We're all on board.

And then we get the data in, we look at it. That will be a big announcement the first time, I think you know, we are able to authorize a point-of-care serology test.

So all the serology tests currently authorized are either for the CLIA high complexity. So the notification path, if a developer has notified us, use the only CLIA categorization or laboratory environment they're allowed to market in and distribute in and use, is in the high complexity lab.

We have authorized some I believe, in the past. At least some moderately complex CLIA category - deemed CLIA categorization. But nothing for point-of-care. Nothing - no home tests yet. And I don't think we've authorized a non-healthcare collection for serology. We're also very interested in that.

So, you know, folks should know that we've not - and that authorization is required for a point-of-care or non-laboratory-based testing and collection. And that - I sent already, quite a few warning letters to folks who have not been following that recommended pathway. And you know, we're continuing to

work on those letters when we find out about that. So you can contact...

((Crosstalk))

Jason Robotham: So I guess, you know, what should we do I guess, as a manufacturer or distributor if we find that, you know, these types of places are offering either our tests or another test in this fashion? You know, I know there's the fraud email that you can send messages to. But doesn't seem like that gets much of a response.

Timothy Stenzel: I can guarantee you that we take all of those seriously. We are - I'm relatively new to the government, having been here a little over two years now.

The wheels of government sometimes don't work as fast as we would wish. We make sure that all our I's are dotted and our T's are crossed. So just because you haven't heard about something, doesn't mean it's not in the works.

Jason Robotham: Okay, great. And just a follow-up in the new temp that was issued. Will there also be a non-laboratory or at-home template becoming available for serology tests?

Timothy Stenzel: Yes. In serology, we're working on three new templates. We're working on a non-laboratory collection which has been - has made the most progress. And then we're working on both a non-laboratory testing situation for serology, as well as, we're working on a recommendation template for a semi-quantitative serology, quantitative serology and neutralizing antibody serology. Those are - all three are combined into one template. And we'll get those out as soon as possible.

Anyone who's interested in developing tests for those situations doesn't need to

wait to interact with us. We'll do our best to work with you. We're going to obviously, to the extent we can, mimic what we've done either in other EUA templates for non-laboratory collection and testing now that the molecular and antigen template for non-laboratory testing is up. And we already had a molecular non-laboratory collection up for a while, now.

There will be some obviously, nuance changes and recommendations on validation. And then when you bring in a new technology like neutralizing antibodies, either correlation with neutralizing antibodies, or actual measurement more directly if they're neutralizing antibodies. That's new technology. We do want to get our arms around how best to recommend that.

But in the interim, we are working with any developers who want to come in for development of those kinds of situations. Okay.

Jason Robotham: Good. Thank you.

Timothy Stenzel: Mm-hmm.

Coordinator: And before we go to the next question, again if you would like to ask a question, press star 1. Unmute your phone and record your name when prompted. And again as a reminder, we are taking one question per caller. Our next question comes from (Ahini Fernando). Your line is open.

(Ashini Fernando): Hello. thanks for taking my call. We noticed that you have added PBS as a specimen transport medium. Do you recommend that EUA tests have to be revalidated with this medium, prior to use?

Timothy Stenzel: I'm sorry, I want to make sure I understand the question. You said, PBS, was the question?

(Ashini Fernando): Yes, PBS as a specimen transport medium.

Timothy Stenzel: Yes. Can you tell me a little bit more details? For example, does it involve non-laboratory collection like in a home? Does it - and is it for an LDT or is it for a kit - a manufactured kit?

(Ashini Fernando): Actually my - where I'm coming from, it's from a global health perspective. So I'm not quite sure where these are collected. But my question is like if it is like in a global health setting when you collect it from patients in PBS?

Most of the test platforms are validated with the wider transport medium. So I'm wondering do they have to be revalidated with the PBS as a transport medium?

Timothy Stenzel: So well from a regulatory perspective how the FDA views this depends. So if it's a lab and they simply want to add PBS or normal saline to what they give their users - their healthcare worker users to use, but it doesn't involve like non-traditional settings like the home, no FDA authorization is required.

If it's a kit manufacturer and they want to claim a normal saline or PBS in their kit they can validate, notify us and send validation data just within 15 business days, to include that into their kit.

And then of course in the non-traditional collection or testing situation - let's talk about collections. The Gates Foundation in partnership with others -- and I'm blanking on all the names -- did validate normal saline. And I forget if they also did PBS. But we pretty much view those as very similar in the non-traditional collection, i.e. home, and did some stability studies in saline.

And any developers that want to utilize that data of the Gates Foundation and their partners, is allowed a right of reference to use that for other applications, as may apply. Toby do you want to add anything to that reply?

Toby Lowe: I think you covered it. Thanks.

(Ashini Fernando): Thank you. It's very helpful to know. Thanks.

Timothy Stenzel: Mm-hmm.

Coordinator: And our next question is from (Eric Deppert). You may go ahead.

(Eric Deppert): Hello. Good afternoon everyone. Is international data acceptable when applying for your EUA?

Timothy Stenzel: Yes, absolutely. That's not a prohibition for those applications and types that are usual. Obviously for serology tests that are amenable to testing at NCI, In addition to what they might do otherwise for their development and validation of that test, we are encouraging folks to submit their tests to NCI for the NCI testing. And it can help us make a great regulatory decision.

(Eric Deppert): Okay, perfect. Thank you so much.

Coordinator: And our next question is from (Tom Slezak). You may go ahead.

(Tom Slezak): Yes, thank you. The recent viral transport media guideline is very clear about what to do if someone is following the standard CDC SOP.

I'd like a little bit of clarification if an international manufacturer has a VTM that is not following the CDC SOP, and how that could be acceptably

validated?

Timothy Stenzel: Toby do you want to take that one?

Toby Lowe: Yes, absolutely. So I'm trying to pull up the guidance right now, to find the right section for you. But there is a section, I think it is IV.B.4. So Roman Numeral IV.B.4, that discusses alternative approaches for additional transport media device types.

And so if you are developing a transport media device that is not validated in accordance with the CDC recommendations, then we would recommend that you follow this section. Which basically, just discusses reaching out to us through the EUA Templates mailbox so that you can provide a little bit more information about your VTM and the validation. And we can consider whether it would qualify for the regulatory flexibility under this pathway.

(Eric Deppert): Okay. Thanks very much on that. I did notice that I'm seeing a lot of the, currently for sale VTMs, that are coming in under a wide range of product codes, many of which are like general-purpose reagents and so forth. Is that something you guys are looking at?

Toby Lowe: As much as we can, yes. So, if there are, you know, devices, VTM or otherwise that you think are being offered inappropriately, please let us know and that information is very helpful for us.

Timothy Stenzel: Great, I've done so, thank you very much.

Toby Lowe: (Great).

Coordinator: And our next question is from (Paul Joseph). You may go ahead.

(Paul Joseph): Hi. Thank you for my call. I had a question about comparing technology with serology COVID test. Essentially, we've run across many companies that are developing technologies, essentially to pair up with a non-CLIA waived serology test at a point-of-care setting.

They essentially take a high-resolution photo of the use of the device and they transmit that with other data points to a high-complexity CLIA lab and they do the confirmation of the results and then they send the data back digitally to the point-of-care with the results of the test.

And I'm curious if there's been any discussions with the FDA about any particular problems with that, if that's something that the FDA would be open to or if there are particular problems.

Timothy Stenzel: So, if the device in question only has a high-complexity designation, all of the testing has to be performed by high-complexity lab, (as far as I know).

(Paul Joseph): Okay.

Timothy Stenzel: However, as that CLIA certificate allows. So, there's potentially close-to-patient situations that can be fast and appropriately monitored by a CLIA high-complexity lab that, you know, might be okay.

Part of (their) point-of-care...

(Paul Joseph): (Do they) ...

Timothy Stenzel: validation involves making sure that lay users, non-laboratory health professionals, can perform testing to get accurate results. So, those devices that

haven't been deemed CLIA waived, should not be used in a CLIA waived environment and we would like to hear about those.

(Paul Joseph): ...okay, that makes sense. And do you think a telehealth component, where CLIA lab personnel oversaw the collection and use of the test? And then the rest of what I just said where the transmission is sent to the CLIA lab personnel for the actual analysis, would that be a potential way to open up these devices to be used at point-of-care with CLIA lab personnel?

(Toby): I think that would - that would be a question for CMS.

(Paul Joseph): Sure, okay, that makes sense.

Timothy Stenzel: And not entirely, I want to add to that. So, we - a device that, the FDA wouldn't view a device, that hasn't gone through all the point-of-care testing validation by non-laboratory personnel, would have concerns, personal concerns about that. But I think (Toby's) right and that CMS should be consulted.

But from an FDA perspective, the appropriate flex studies for use by non-laboratory professionals, you know, a laboratory professional can pipette and we know that they can pipette that accurately.

It's hard, by telemedicine, to know that the pipetting done somewhere else by non-laboratory personnel is done accurately, even via telemedicine.

So, we appreciate all the creativity that's being applied to the situation, use of telemedicine is - in health, is greatly encouraged and there are appropriate uses. And sometimes because of the presence of telehealth and telemedicine, and the mitigations of the involvement that way, we can reduce some of the opportunities to validate. We can - it is a risk mitigation, but it doesn't

necessarily mitigate all risks.

So, we would point all developers to our serology template that has point-of-care validation information, and now the new molecular and the direct antigen test, have those studies as well on the template. And then a new - an update on the molecular update now has for molecular point-of-care recommendations for validations.

So, validations performed that way are very important for situations where it's non-laboratory personnel carrying out testing. Okay?

(Paul Joseph): Great. That was very clear. I appreciate your help. Thank you.

Coordinator: And our next question is from (Arita Dapati). You may go ahead.

(Arita Dapati): Yes, thank you very much. I'm looking at the new non-lab use template. You mentioned that the manufacturers can enroll known positive patients into a performance evaluation study. However, in our recent interactions with FDA for a POC use indication, for rapid antigen assay, FDA has been pushing back on the enrollment of known positives to our clinical study. It seems like a contradiction. Can FDA please comment to confirm that the study enrichment via enrollment with known positives is okay for a POC use indication?

Timothy Stenzel: In particular, you're asking about use of bank samples for point-of-care assessment, is that - and securing, I would guess, positives?

(Arita Dapati): They're actually not banked, they're being collected at a recall site, so they're being enriched with positives.

Timothy Stenzel: Yes, well, we're trying to be consistent across the board. And as we evolve here,

we want to maintain flexibility. Our recommendations in writing are, you know, are that, our recommendations. And if there's any particular technologies, there's any alterations to thoses recommendations, review, I encourage communication with the FDA to limit potential additional testing that may be necessary for an authorization.

So, we understand that sometimes it's difficult to get samples. We've moved away from contrived samples for the most part and into actual POC samples. We understand that there could be challenges in getting fresh, on the spot samples. So, we do remain open to alternate assays, but I would say that, you know, if you're going to alter from a recommendation, I encourage you to discuss that with the FDA.

(Arita Dapati): Okay, yes, these are fresh, on-the-spot samples. It's just that they're being gathered at a recall site where folks that have already been tested as positive are being recalled to do a secondary test with our device as well as a PCR.

Timothy Stenzel: So, I think what you're saying is can - okay, I'm just trying to understand a bit. I think what you're saying is, in order to limit the size of the study, can you have a screen first on another test to know which patients are positive and then come in - and have those patients come in and be tested so that you can have a little bit more focused clinical study and design...

(Arita Dapati): Yes, that's correct.

Timothy Stenzel: ...as many people. So, we were - so, I understand now. As long as the comparative test is a good test. I don't see a huge amount of challenges with that. There are a couple things we'd want to make sure that the person that's re-testing the patient is not aware of the previous results.

So, and, you know, and then once you bring those patients in and have the person performing the test be unaware, that is important. I think if they know those settings are going on and being recalled, then they would assume that patient was basically positive and they'll be looking for the positive results on that patient and we don't want to do this bias in this study, so that's important to control that balance and that's the sort of thing that you can discuss with the FDA.

But comparative testing is very important, but it'd be a really good test. We are starting to see some variabilities of sensitivities of tests. We always try to alert the public and users about these things, but there will be performance differences and we really want comparative tests to be a good test.

So, I'll just say that we continue to see developers use tests like the Abbott ID NOW as the comparative and we stated on this town hall call before that it's probably not a good thing to do to use the Abbott ID NOW. There's some of the issues that we've publicly stated about some concerns about that device.

By the way, we continue to monitor that situation closely, but it's not a good comparative device for a molecular comparator as required.

So, what I'm saying is that the devil’s in the details for the study design that you're talking about. I don't see any show-stoppers, we just want to make sure that there isn't a bias introduced into them.

There may be additional mitigation that we'll look into, you know, and that could be weaved pre-market or it can be considered post-market. If you continue to have challenges with this with talking to any of our team members, you know, be happy to ask for Dr. Stenzel to get involved in working out some of those details if you want.

(Toby): Yes, I'd also add that if you want to send an email to the templates email box, you can have further questions about this specific to your testing, to your questions because the - while there is information about point-of-care testing in the antigen template currently, it is not very detailed, and so we can provide some additional discussion on that for you.

(Arita Dapati): Okay. Thank you so much, it's really appreciated. Yes, we're looking at using the Abbott real-time and doing - and so we'll reach out to both the templates email as well as to Dr. (Stenzel) to look into the - whether we need, a mix of positives and negatives, recalled, or just positives.

Timothy Stenzel: I would ask that if you - if you - if you're getting pushback from some of the folks in the FDA, we just want to try to figure out a way forward, I'm happy to get involved, but our team is great and most of the time they can help you without my help and that would be greatly appreciated too. All right, thank you.

(Arita Dapati): Sure, understood. Thank you.

Coordinator: Our next question is from (Dejia DeCall). You may go ahead.

(Dejia DeCall): Thank you for taking my questions. My question is around the multi-analyte respiratory panel. So, what we have been getting, these unapproved samples for those tests, primarily PBS, saline, e-swab, and whatnot, but they are paired with SARS-CoV-2 assay, and we're getting a lot of complaints from our (citizens) that they would have to collect two different types of collection device VTM for these multi-analyte respiratory panel and they can collect anything else for others.

So, my question to you, is FDA going to give us some guidance on how to deal

with this kind of situation on those large respiratory panel assays to accept these sample types that have not been approved by FDA?

Timothy Stenzel: So, I mean, if they're standard sample types and the media is just different, I think our answer - Toby you can correct me - but I think our recommendations are that you validate that per your normal laboratory procedures and, basically, to CLIA expectations and standards if you're a lab, and that we encourage you to, even they - so they are not commonly or validated specifically, you know, rather than VTM against normal saline or PBS.

Or, you know, another manufacturers VTM that may not, we do encourage that you try your best to test those samples and report out the results. You know, we realize that the laboratory expertise can really make a big difference here in understanding what's, you know, what you're willing to accept and making and ensuring in - within your CLIA quality system what you're comfortable with doing.

And also, you know, with you basically controlling all the testing and the interpretation on all that, knowing when there might be a problem with a particular sample and exercising due caution on those.

But from an FDA perspective - and (Toby) you can add to this if needed - that kind of difference, we would not require an EUA submission for - to see, you know, saline versus VTM, for example, that's not - it's just something that we think one of these flexibilities, adaptability, regulatory tier that - now if someone wants to validate and send us data for valid EUA authorization that's fine to - we're always open to that, but (Toby)?

(Toby): Yes. I think that all depends a little bit on how the test is authorized, whether the authorization is specific to the type of sample that has been validated and

authorized. And, you know, generally, we think that it's important, you know, for validation to be completed for whatever - whatever testing is being done.

And, you know, particularly for the multi-respiratory panels, we don't, you know, we haven't seen as much with different specimen types. So, we would encourage you to talk to us about what you're looking to do there.

(Dejia DeCall): Okay, great. Thank you. And I didn't want to bring the bad names, but I guess I'm going follow up with it, BioFire, Luminess, and GenMark, they have 20 or so analytes. And from our laboratory point-of-view, we'd have to do some sort of validation here in the lab for using that as a off-label use of FDA approved tests and all of those are nasopharangeal specimen type and VTM.

But for VTM, that's why we would be using off-label, here in the lab and validating 20 analytes on a smaller lab which runs on (unintelligible) sample (to answer) format is going to be quite a challenge for us because we'd have to go back and verify the (LoD) and whatnot, if we're following the right procedures.

So, I would really like to get FDA's help on this because there are many, many smaller labs that focuses on the sample to answer format and getting the results out without doing all these laboratory developed assay type of validations. So, that's where I'm coming from. Thank you, again.

Timothy Stenzel: Yes, so, I think that's a good thing to take back, Toby. I mean, certainly, I think we've provided flexibility to allow, you know, FAQ's, perhaps we can expand that a little bit. You know, making recommendations about how a lab might validate that for their own purposes is a scientific question that, you know, I don't know that the FDA is, you know, prohibited from joining in on.

So, I think if labs are wanting some additional, say, recommendations on

validations, it's something we need to take back and consider.

(Dejia DeCall): Okay, that would be highly appreciated. Thank you.

(Toby): I think I'd also add that the regulatory flexibilities that we've provided, you know, as outlined in our guidance, are related to SARS-COVID-2 testing only. They're not - they do not apply to multi-respiratory panel.

(Dejia DeCall): Correct. The problem is the, you know, the VTM is not available in the market so people are using whatever they can find. Same thing for the lab, and we reject them and they are very unhappy. But this is only - this - we are in summer, but when the winter hits out, it's going to get a million times worse. And so, I'm kind of trying to think ahead of how to prepare the lab, for year, in dealing with the respiratory (unintelligible).

(Toby): Sure. And we're hoping that...

((Crosstalk))

(Toby): ...yes, yes, I think we're hoping also thatthe VTM guidance that we just put out, will help with some of those availability issues.

Timothy Stenzel: Yes. We do know that the COVID situation doesn't divide cleanly from COVID testing and non-COVID testing in a number of different ways. So, you know, for example, if you even sourced new tips for a robot or something, you know, it, you know, it's a robot you use for all sorts of testing, COVID and non-COVID testing.

What you do for COVID and the impact of COVID has impact on all the laboratory testing. So, we have begun these dialogues internally and with others

about how we deal that situation. You're - you bring up a great example of how - of how everything can - and at some points be interconnected here, and the agency and FDA wants to take a holistic view and be as helpful and friendly and flexible as possible here in this situation.

So, I thank you for bringing that up that point.

(Dejia DeCall): Okay, thank you.

Coordinator: Our next question is from (Kay Jewell). You may go ahead.

Timothy Stenzel: Hi, (Kay)...

((Crosstalk))

Coordinator: And (Kay Jewell), your line is open, we're not able to hear you. And we'll go to our next question from (Bridgett Patell).

(Kay Jewell): Sorry...

Coordinator: You may go ahead.

Timothy Stenzel: (Kay)?

Coordinator: And (Bridgett Patell), your line is open, we're not able to hear you.

(Bridgett Patell): Hi, good afternoon, thanks for taking my call. My question is concerning the enforcement policy on viral transport media which is published recently. Is that still a validation? This policy states that is important that the VTM are appropriately designed and validated prior to distribution to ensure that the

transport media will preserve the viral particles without meaningful deterioration that could lead to inaccurate test results.

To reduce the risk of inaccurate test results, only VTM devices labeled as sterile should be used in the transport of the clinical specimen and FDA believes that the VTM distributed by commercial manufacturer under the policies that we've designed and validated consistent with the CDC SOP.

So, could you please clarify with respect to validation, when designed and validated in accordance with the CDC SOP would mean validation of sterility only? Or, would it mean the validation of sterilization process and performance testing that demonstrate the viral particles in clinical specimens and (then the virus is detectable)?

At this point, we're unsure of the validation in this policy requires and we'd really appreciate any clarification from you on this.

(Toby): Sure, sorry about any confusion there. So, that is indicating - that is what we expect for validation, not just for sterility, but for the VTM as a whole. We would expect the VTM to be designed and validated consistent with the CDC SOP.

(Bridgett Patel): Okay. So, that means the performance testing –as well as performing some LoD testing and all of that, correct?

(Toby): That's correct.

(Bridgett Patel): Okay, thank you.

(Toby): No problem.

Coordinator: And the last question is from (Jore Barren). You may go ahead.

(Jore Barren): Yes. So, I want to ask about pooling and in particular, I understand the current guidance is for pools of up to size 5. And, of course, there are a lot of algorithmic methods that can improve the robustness when looking at test results from multiple pools together. And I'm wondering whether there's been any FDA thought about allowing to pool at larger sizes provided that there's an algorithm that can account for the possible lesser quality?

((Crosstalk))

Timothy Stenzel: That's a good question.

(Toby): Go ahead.

Timothy Stenzel: That's a good question. We don't limit the pool size to 5. It all depends on the situation and the validity of the data, but if you're able to verify a larger pool. We also don't specify the type of pooling. We have provided a little bit more information say on, if you want to pool swabs rather than pool VTM, you can do simple Dorfman pooling.

You can do matrix pooling as I believe - well, we've authorized, I think, some matrix pooling or, I think, thinking about if it's simple matrix where it’s basically, you know, you just, you know, read the rows in the columns and you can identify the sample that way.

There are also what I call more complex or combinatorial pooling which I think you're talking about. Realizing, though, that the more complicated the pooling is, particularly when you move into combinatorial pooling, the percent typically

when you do it, that the percent positive efficiency goes down, right? So, if you want to maintain good efficiency on what you're - based on what your percent positives are in your population, it can go - it can go way down.

So, I've seen some published, mainly theoretical papers on combinatorial pooling where really anything over 1.3 positivity in your population didn't justify that combinatorial pooling.

So in the situation where we have very low percent positivity, those kind of pooling algorithms work best.

(Jore Barren): Okay. So, is there somebody at CDC that we could be - CDC, FDA, any of the government agencies that we could be in contact with and would be able to, kind of, provide direct - direct responses to some of our technical questions?

Timothy Stenzel: Yes. So, have you reached out to the FDA through our template email address or with the pre-EUA? And what we call pre-EUA is simply taking one of our templates and putting some information in there and submitting it to us as a pre-EUA that can - it's a framework for allowing us to begin dialogue and everything's documented and tracked.

(Jore Barren): Okay, can do that.

Timothy Stenzel: All right. Great.

(Toby): And just to briefly add, if you haven't yet seen the update to the template that was put out yesterday, it does include a little bit more information on the different pool sizes and the correlation between the positivity rate and the efficiency.

(Jore Barren): Thank you very much.

Timothy Stenzel: But that's just for simple Dorfman pooling. With the combinatorial pooling which, you know, obviously there's potentially millions, infinite number of ways to do - accomplish variable pooling, and we did not provide efficiency calculations for that, that depends on your algorithm and the number - the size of the pools that you have within there and how many times you retest and you'll sample within different pools.

(Jore Barren): Okay. I'll look into those resources and get in touch. Thanks a lot.

Timothy Stenzel: Great.

Coordinator: And that concludes the Question and Answer session. I'd now like to turn the call back to Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will be available on the CDRH Learn webpage at www.fda.gov/Training/CDRHLearn, by Tuesday August 4th. If you have additional questions about today's presentation, please email, CDRH-EUA-Templates@fda.hhs.gov.

As always, we appreciate your feedback. Following the conclusion of the presentation, please complete a short 13 question survey about your FDA CDRH Virtual Townhall experience. The survey can 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: And this concludes today's conference. Thank you for participating. You may disconnect at this time. Speakers, please stand by for post-conference.

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