Virtual Town Hall #90
August 24, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kimberly Piermatteo: Hello and welcome everyone to Virtual IVD Town Hall Number 90 for SARS-CoV-2 test developers in which we'll discuss and answer your questions about diagnostic tests in response to COVID-19. Thanks for joining us today. This is Commander Kim Piermatteo of the United States Public Health Service, and I am the Education Program Administrator within the Division of Industry and Consumer Education in CDRH's Office of Communication and Education. I'll be your moderator for today's Town Hall.

Our panelists for today's Town Hall are Toby Lowe, Associate Director for Regulatory Programs in the Office of Health Technology Number Seven, or OHT7, in CDRH's Office of Product Evaluation and Quality, or OPEQ. Joining Toby today is Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices, also in OHT7.

For today's Town Hall we'll begin with opening remarks, followed by answering your previously emailed questions and then proceed to address your live questions.

A recording of today's Town Hall and transcript will be made available on CDRH Learn under the section titled Specialty Technical Topics, and then the subsection titled Coronavirus COVID 19 Test Development and Validation Virtual Town Hall Series.

The July 27th IVD Town Hall recording and transcript have been posted.

We will continue holding these Town Halls monthly on the fourth Wednesday of the month. Therefore, the next scheduled IVD Town Hall will be on Wednesday, September 28th, 2022 from 12:05 to 1:00 PM Eastern Time, followed by one on October 26th. Future dates for town halls after that will be announced once they have been confirmed. And please refer to the virtual Town Hall series web page for details on upcoming Town Halls. A link to this web page has been provided at the bottom of the slide.

And lastly, I do have two administrative reminders today. First, for those of you participating live in today's Town Hall, please be sure you have joined the Town Hall via the Zoom app and not through a web browser to avoid any technical issues. And secondly, I will lower all raised hands at the beginning of our previously emailed questions segment. If you have a question for today's Town Hall, please raise your hand when I indicate that we will now take your live questions.

I'd now like to welcome Kris, who will provide today's opening remarks. Kris, the floor is yours.

Kristian Roth: OK, thanks so much, Kim. Appreciate it. So I think the main update we want to give for today is to highlight the safety communication that was published on the FDA website on August 11th. The title is here on your screen "At-Home COVID-19 Antigen Tests-Take Steps to Reduce Your Risk of False Negative Results." In that communication are recommendations for an increased level of repeat testing with COVID antigen tests. This is both for symptomatic and asymptomatic individuals.

For individuals that are asymptomatic, we recommend testing a total of three times with 48 Hours between tests to confirm a negative, to provide a negative result. Of course, any positive in that time

frame is a positive result and no further testing is needed. And also, for symptomatic individuals, we are recommending testing two times, again 48 hours apart, to improve the performance of those tests for negative results.

There are two preprints which are referenced in the safety communication. These preprints provide the basis for these new recommendations. One is the study protocol and the other one is an analysis of the data. These were broken up into two different publications because the protocol is fairly detailed and does take a novel approach. And it was, in and of itself an interesting study protocol.

We believe that these data support a recommendation to test multiple times over multiple days when using a COVID antigen test. This was a relatively large study performed with three commonly available COVID rapid antigen tests. And we do believe that the results of the study can be leveraged by other manufacturers to address the current condition of authorization which discusses serial testing.

In the coming weeks, we will reach out to all antigen test manufacturers with additional information on this approach. We believe that it is critical for public health that these tests remain on market. We'll work with manufacturers to ensure that tests remain available and any changes which are needed to the labeling are rolled out in a predictable and transparent manner. More information will be available soon, and we will provide updates on this call throughout this transition period.

And that's all I had for the announcements.

CDR Kimberly Piermatteo: Great. Thank you, Kris, for those opening remarks. We will now answer your previously emailed questions.

Please note, as always, we do receive some questions that are too detailed or test-case specific that we will not address today. For those questions, we will try to send a response in writing within a few days. If you have submitted a question and do not hear it addressed today, please look for a written response. If you do not receive a response within a few days, please feel free to reach back out to the CDRH-EUA-Templates@fda.hhs.gov mailbox for an update.

Toby, I'll be directing these questions to you. The first question has two parts. And the question is, the first part, "Is FDA currently accepting EUA requests for multiplex antigen tests that can detect a combination of viruses, for example, SARS-CoV-2 and influenza, intended for use in an OTC setting?". The second part of that question is "For a multiplex molecular test with both flu and COVID, is it required to have a separate call for both flu A flu B in addition to COVID, or is it acceptable to combine flu A and flu B into a general influenza call?".

Toby Lowe: Thanks, Kim. So we have authorized several antigen multi-analyte diagnostic tests intended for use at laboratory and point of care sites. We currently do not have any multi-analyte over-the-counter tests authorized, but we do have recommendations in the appropriate template, and these types of tests do meet the current priorities. We've noted here before that if you're considering an over-the-counter multi-analyte test, we recommend that you submit a pre-EUA to further discuss your test design and proposal.

Regarding the flu and COVID and the separate calls for flu A and B, there are numerous flu A/B rapid antigen tests on the market, and all of those differentiate between flu A and B. So our current

recommendations are in favor of reporting a separate flu A and B result because the risks and benefits of flu A and B results are different.

CDR Kimberly Piermatteo: Thanks, Toby. Our next previously submitted question is, "Was it FDA's intention to exclude administration of an over-the-counter COVID test by a health care provider so that swabbing by a health care provider would constitute off-label use?".

Toby Lowe: No, I think this is a misunderstanding or a misread of the labeling. All home-use tests are authorized with home-use instructions and health care provider instructions. And the intended use typically states something along the lines of, this test is also authorized for non-prescription home use with self-collected anterior nasal nares swab samples from individuals aged 14 years or older or adults collected anterior nasal samples from individuals aged two or older.

So there is no restriction on adult collection. Any adult can collect a sample from an individual aged two or older. And the worded of two or older, and not two through 14, to include those health care provider collections as well as others.

CDR Kimberly Piermatteo: Great. Thanks again, Toby. Our next previously emailed question is "Should COVID antigen test developers start a study to address their serial testing condition of authorization?".

Toby Lowe: Thanks, Kim. So this goes along with the announcement that Kris made at the beginning of the call. We do include information about the UMass study and data in the safety communication that Kris mentioned. And we've previously discussed these serial-testing studies on this call before, and our current position remains that developers are free to start a study to address that condition of authorization, but we are currently not recommending that developers perform those studies since the preprint that's described in the safety communication describes a study that's sufficient to establish performance in an asymptomatic population.

CDR Kimberly Piermatteo: Alright, thanks Toby. Our next question has three parts. I'll read through them, and then I'll turn it over to you, Toby. So the first part is "Is it too late to submit a pre-EUA to FDA for review?". The second part is "If the EUA pathway ends soon, can the submission be converted to a 510(k) as long as more data is provided?". The third part is "Will FDA publish a draft guidance for this?".

Toby Lowe: Thanks, Kim. So this topic has come up on the Town Hall a number of times. And it is not too late to submit a pre-EUA or EUA request for FDA review. We recommend that you take a look at the test policy guidance, that is on the bullets on the screen right now, to make sure that your test fits within the current FDA priorities. And as we've discussed on the town halls previously, we cannot anticipate when the public health emergency will end, but we are working on a transition plan for devices that are offered under EUA.

In December, FDA issued the draft guidance transition plan for medical devices issued EUAs during the COVID-19 public health emergency. That was put out as a draft guidance for comments. And since the guidance was issued in draft for comment and not for implementation, if there are points about that guidance that are unclear, we recommend that you submit a comment to the docket indicating any areas that could benefit from additional clarity.

And if you have a question about how to manage your current plans for moving forward now with your emergency use test or with a 510(k), we recommend that you send an email to the EUA templates mailbox with sufficient details so that we can provide appropriate feedback.

And then finally, unless revoked, EUAs are in effect until the public health emergency 564 declaration is terminated. This typically does not happen for quite a while, and that can be seen for previous emergencies that still have not been terminated, such as Zika and Ebola.

CDR Kimberly Piermatteo: Thanks, Toby. Our last previously emailed question is "Has FDA authorized SARS-CoV-2 diagnostic breath tests?".

Toby Lowe: Yes, we have authorized one, that is the InspectIR COVID-19 breathalyzer, that analyzes breath samples for SARS-CoV-2 detection. And information about that test can be found on our website on the EUA Other Tests for SARS-CoV-2 web page. And anyone who is interested in submitting an EUA request for additional breath tests can take a look at the information, authorization documents for that authorized test to see what data we looked at for that one.

CDR Kimberly Piermatteo: Great Thanks, Toby. So that wraps up our previously submitted question segment. We will now take your live questions. So to ask a live question, please select the Raise Hand icon at the bottom of your Zoom screen. When you are called on, please follow the prompt in Zoom and select the blue button to unmute your line. Then identify yourself and ask your question.

Please remember to limit yourself to asking one question only. If you have an additional question, you may raise your hand again to get back into the queue, and I will call on you as time permits. And please remember, we are not able to discuss specific submissions under review.

Alright, our first live question is coming from Anjali. Anjali, I'm going to unmute your line. Please unmute yourself and ask your question.

Anjali Zimmer: Hi there. Thanks for taking my question. And it's a little off topic so apologies. But you've been speaking about monkeypox on the top of the call the last few months, so I was wondering if FDA had any comments about possibility for a EUA pathway on monkeypox diagnostics and collection devices.

Toby Lowe: Thanks for that question. We don't have any specific updates here other than I think has probably been mentioned previously. We are interested in working with developers on monkeypox tests, so please feel free to send in, we can always accept pre-EUAs, even prior to the declaration of a 564 emergency for EUA for the use of the EUA pathway. And so we're happy to engage with developers Kris, I don't know if you want to add anything there.

Kristian Roth: No, thanks

Anjali Zimmer: Thank you.

CDR Kimberly Piermatteo: Thank you, Anjali. Alright, our next question is coming from Homer. Homer, I have unmuted your line. Please unmute yourself and ask your question.

Homer Wu: Hi, this is Homer Wu from Hopkins MedTech Compliance. Thanks for taking my call. We actually have a question regarding to multi analyte. It's COVID-19 plus flu A and flu B. It's a OTC device. And we actually submitted a pre-EUA before. It kind of took us almost four months get some answer, but we still have a question regarding to flu B. I guess in previous call that FDA allowed us to do the flu B clinical study in other countries, for example South American countries.

My question is, first, is that still the case? And if that's so, can we do the flu B study in South American country, or do we have to bring the sample to the United States? So that's my question.

Kristian Roth: OK. Let me see if I understand here. So you have two questions, one, can you perform a clinical study in an outside the U.S setting? And then number two, you're talking about taking the samples from OUS setting, shipping them to the U.S. for testing?

Homer Wu: What's the option, whether we can do the study, I believe we want to do a prospective flu B study, so we do find subjects in other countries, for example Mexico, right? Can we actually conduct the study over there? Right? So we do the prospective, we can do the self-test there, and we do the lab test there. Or do we have to bring the sample to the United States for either self-test or the lab comparator test?

Kristian Roth: OK. Certainly, there's no requirement to do the testing in the U.S. for the comparator method. OUS studies are tricky. And especially if you were designing a test for over-the-counter use, we want to ensure that that setting is similar to a setting that a typical user in the U.S. would experience. So I think we're open to the proposal, but there are certainly more details than we could cover here. So again, I would recommend sending a supplement to that pre-EUA. If you've got a proposal and some specific questions, we're glad to address that in a supplement.

And just to comment on the time frame a little bit, the more detail and the more focused questions that you provide in a pre-EUA, the better we can answer your questions and the quicker we can answer your questions. Just asking us for a study design for OUS for flu B, that's going to be a little bit more difficult and take much longer for us to answer. So if you've got really targeted questions, specifically about a study design that you have planned, we're glad to accept that in a pre-EUA.

Homer Wu: Oh, I'm sorry. I just want to clarify. We did submit a pre-EUA. That was closed. Now we can do a supplement to that pre-EUA, right?

Kristian Roth: Yep, I would just reference the previous pre-EUA and say, hey, we've got additional questions or some other sort of detail, and just submit that as a supplement to the original one.

Homer Wu: OK, that's great. All right. Thanks a lot.

CDR Kimberly Piermatteo: Thank you Homer. Thank you Kris. Our next question is coming from Seungjin. I have unmuted your line. Please unmute yourself and ask your question.

Seungjin Ha (Gina): Hi, how are you? This is Gina from Seungjin. And our company is developing the influenza A and B with COVID-19 detection antigen testing kits under the FDA EUA process. And the other one, we are also developing for the influenza A and B, also antigen testing kits under the FDA 510(k) process. But we are trying to conduct a clinical trial with those two testing kits under the same procedure at the same time by the IRB operable with the clinical trial protocol.

So I would like to know, if we collect one swab sample from our patients and it will be added into the reagent tube and containing the extraction of buffer. And also, we will use this one swab and one extraction buffer to the two kits at the same time. So we would like to know if it is possible for clinical trial with these two kits at the same time under the IRB approval. Do you think it is available or acceptable by your side?

Kristian Roth: Yeah, thanks for that. It's a little bit of a challenge because you are using the test kind of off label or not with the instructions that folks will have if it's either the COVID/flu combo or the flu alone. That being said, we do want to try to make efficiencies available to developers where it's appropriate. And so I think probably you're going to want to submit this as a pre-EUA and let us know what the volumes are, what the challenges are, what happens if they run out of volume on the second test or something of that nature.

And then I would also maybe think about a backup plan as well. So propose a sampling plan of, we'll do the standard care first, then we'll do the flu/COVID next, then the flu alone, and some sort of randomization scheme. So I would just plan for both instances or provide us a plan, I guess, in both instances, one, using the same abstraction buffer and two, provide a sampling plan that minimizes bias for the two candidate tests.

Seungjin Ha (Gina): So you recommend we have to get through the pre-EUA for those submissions?

Kristian Roth: Yeah, I wouldn't be able to comment. I can't say on the phone, yes, it's fine to use the same abstraction buffer. One, it's off-label use to use against the instructions for use. And number two, we'd be concerned about running out of buffer.

Seungjin Ha (Gina): OK. I got it. So before we are going to conduct the clinical trials with these at the same time, clinical trials, we have to get through the pre-EUA and FDA should have reviewed our clinical trial first before removing every bias for conducting this clinical study. Am I correct?

Kristian Roth: That would lower your risk. Of course, if we know what you're going to do prior to you doing it, then you've got buy in from us, and you can be confident that your sampling plan is kind of agreed upon. Of course, that's not a requirement. You can go off and do your study, and then we can review it after it's done. But that's a little bit more risk on your end.

Seungjin Ha (Gina): Yeah, I understand. OK, thanks.

Kristian Roth: Thank you.

CDR Kimberly Piermatteo: Thank you Gina and Kris. At this time, I'm going to ask if anyone has any questions to please raise your hand. OK we have a question from Kay. Kay, I have unmuted your line. Please unmute yourself and ask your question.

Kay Taylor: I just wanted to ask a clarification on the information from the August 11 safety communication and the upcoming changes to instructions for use. Is that applicable just to the at-home antigen COVID tests? And the reason I'm asking, there's been a little bit of confusion on whether that is applying to the professional-use COVID tests, which are typically only for symptomatic testing.

Kristian Roth: Sure. Yes, thanks for that, and sorry about the confusion. However, we haven't officially released our plan yet. Once we do, we plan to communicate with all antigen test developers at the same time to make sure that everyone who, potentially, could be impacted kind of knows what the strategy is, like I said, at the same time. So that is part of a communication plan. We're still discussing what the path forward is for everybody. And once we have that finalized, everyone should know.

Kay Taylor: OK. Thank you.

CDR Kimberly Piermatteo: Thank you Kay for that question. We have another question coming in from Richard. Richard, I have unmuted your line. Please unmute yourself and ask your question.

Richard Montagna: I'm Richard from [AUDIO OUT]. We have previously submitted both in silica and wet lab testing against the BA.5 variant. It's been probably 10 days or so since we submitted the wet lab testing. We haven't heard anything. Should we expect to hear something that FDA accepted our conclusion? Thank you.

Kristian Roth: Sure. That's fair. I can catch up with the variant team and make sure that you get a response. Usually, no news is good news.

Richard Montagna: Yeah, that's what I think.

Kristian Roth: But I can appreciate you want a positive response, and we can get that out too.

Richard Montagna: OK, thank you very much.

CDR Kimberly Piermatteo: Thank you, Richard. Thank you, Kris. Alright, I will make one last call out. If anyone has any additional questions, please raise your hand at this time. OK. Kay, you have another question. I have unmuted your line. Please unmute yourself and ask your question.

Kay Taylor: Sure, thanks, since we have the extra time. My question is more along, I'm sure FDA is fully aware of the low prevalence of flu B this season, even outside of the United States. With some of the professional triplex antigen tests for COVID and for flu A/B, are there discussions going on within FDA for how companies continue to try to meet their post-authorization commitments to have a performance study? Are there discussions about how long companies should continue to try to acquire samples for flu B, primarily?

I just was curious if that is a topic that's being discussed at FDA. And maybe there will be some guidance coming cause I know FDA is looking for actual patient samples and not really wanting, at this time, to accept contrived samples. But is that something that might be on the horizon at some point where if we just can't get native flu Bs that some other surrogate-type sample might be accepted?

Kristian Roth: Sure. Thanks for that. I completely understand. We're thrilled that there's no flu B out there to get sampled, honestly. I know it's a challenge for test developers, but with COVID kind of persisting and now potential monkeypox, it seems like if flu B stays low, it's best for everybody in public health, certainly.

There should be a time limit on that condition of authorization. And that suggests whatever data you have within that time limit, you should come back to us and let us know what you have and what efforts

are ongoing. We're well aware that there's no flu B, and we don't necessarily have a plan to go with contrived samples. Really, we are going to continue to recommend live samples. But again, you can submit that within the time frame and have that discussion with your lead reviewer. They would be the ones that know your test best and know the current path forward for flu B.

Kay Taylor: OK. Thank you.

CDR Kimberly Piermatteo: Thanks, Kay. Thanks, Kris. Alright, we have no more raised hands at this time, so I'm going to move to close today's Town Hall. I appreciate everyone's participation today, and I thank Toby and Kris for serving as our panelists.

As I mentioned earlier, a recording of today's Town Hall and a transcript will be made available on CDRH Learn within a week or two of today. You will find the recording and transcript under the section titled Specialty Technical Topics, and then the subsection titled Coronavirus (COVID-19) Test Development and Validation Virtual Town Hall Series. To access those materials, please visit CDRH Learn at the link provided on this slide.

For additional questions about today's Town Hall and COVID-19 IVD topics in general, you may send an email to CDRH-EUA-Templates@fda.hhs.gov.

And please remember to join us for our next Town Hall, scheduled for Wednesday, September 28th, 2022 from the same time, 12:05 to 1:00 PM Eastern Time.

Thank you all again for joining us, and this concludes today's Town Hall. Have a great day.

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