CDRH Virtual Town Hall #96
Monkeypox and COVID-19 Test Development and Validation
October 26, 2022

CDR Kim Piermatteo: Hello and welcome everyone to today's Virtual Town Hall number 96 for monkeypox and SARS-CoV-2 test developers. Today we will discuss and answer your questions about diagnostic tests in response to the monkeypox and COVID-19 public health emergencies.

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 Virtual Town Hall.

Our panelists for today are Dr. Timothy Stenzel, Director of the Office of In Vitro Diagnostics, which is also referred to as the Office of Health Technology Number 7, or OHT7 in CDRH's Office of Product Evaluation and Quality, or OPEQ. Joining Tim is Toby Lowe, Associate Director for Regulatory Programs in OHT7 and Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices in OHT7, and Dr. Noel Gerald, Branch Chief for Bacterial Respiratory and Medical Countermeasures in OHT7 as well.

For today's Virtual Town Hall, we'll begin with opening remarks, then we'll answer your previously emailed test development and validation questions about monkeypox and COVID-19, and then lastly, we will address your live questions.

As a friendly reminder, for those of you participating live in today's Virtual Town Hall, please be sure you have joined us via the Zoom app and not through a web browser to avoid any technical issues.

We will begin-- or sorry, we will be holding Virtual Town Halls on November 9 for monkeypox test developers specifically, and then on November 30 and December 14 for both monkeypox and COVID-19 test developers. You may refer to our web page titled “Medical Device Webinars and Stakeholder Calls”, specifically, our “Virtual Town Hall Series - Test Development and Validation During Public Health Emergencies for COVID-19 and Monkeypox” webpage for details on all upcoming Virtual Town Halls. Links to both these web pages have been provided on this slide.

Next, I also wanted to let you know we have posted the presentation and transcript for our last Virtual Town Hall for monkeypox test developers, which was held on October 12, 2022. We have made some recent updates to our Virtual Town Hall series webpage. And I specifically wanted to draw your attention to an important update, which is that all previous and future Virtual Town Hall series materials, that includes presentations, printable slides, if applicable, and transcripts, are and will be available on CDRH Learn under the newly created section header titled “In Vitro Diagnostics” and then under the subsection titled “Virtual Town Hall series.” I have provided a screenshot of CDRH Learn where you can find these materials on this slide.

I'd now like to welcome Tim, who will be providing today's opening remarks. Tim, the floor is yours.

Timothy Stenzel: Thank you, Kim. I got a bit of laryngitis today. So if I lose my voice, I have tremendous backup on the call. With Toby, Kris and Noel. Noel of course, has been heading up our monkeypox response effort. And he's been doing a really tremendous job on that.

So hopefully you can hear me well enough. And hopefully my voice lasts through the town hall today. The good news about monkeypox is that numbers continue to trend down worldwide and in the U.S. In the U.S., we are now at 15% of the peak that we saw earlier in the U.S. But of course, we're only going to be happy when that number goes to zero. And with that, I think Toby's up next. He's going to cover another agenda item, and then we'll go into the previously submitted questions. Thank you.

Toby Lowe: Great. Thanks, Tim. So we just have one update about monkeypox. We have posted on our website the notification list of the lab developed tests that have notified FDA as described in the policies under sections IV.A.2, IV.A.3, and IV.C in the policy for monkeypox tests that was issued in September. So we have those available on our website if anyone needs to reference those lists. And with that, I think we can head into the questions.

CDR Kim Piermatteo: Thank you Tim and Toby for those remarks. We will now answer your previously emailed questions about monkeypox and COVID-19 test development and validation. As always, please note we do receive some emailed questions that are too detailed or test case-specific that we will not address during today's Virtual Town Hall. 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 MPXDx@fda.hhs.gov mailbox or the COVID19DX@fda.hhs.gov mailbox for an update.

So Toby, I'll be directing these first previously emailed questions about monkeypox test development to you. The first question is a two-part question regarding a clinical study using retrospective natural clinical specimens. So the first part of that question is, can an EUA-authorized monkeypox test be used for discordant analysis between the candidate device and the CDC test?

Toby Lowe: They can. As noted in the molecular diagnostic templates, we do recommend establishing a discordant analysis plan prior to your clinical studies. Excuse me.

Discordant samples should be tested with an EUA-authorized PCR test that has been validated for the same type of clinical specimen, has demonstrated high sensitivity, and uses a chemical lysis step followed by solid phase extraction of nucleic acids, such as silica bead extraction. And this is all discussed in the template. And we should also note that results from a discrepant analysis should not be included in the calculation of NPA and PPA but may be added to the performance table as a footnote.

CDR Kim Piermatteo: Thanks, Toby. Alright, the second part of that question is, per the FDA's template for developers of molecular diagnostic tests for monkeypox, the clinical evaluation section recommends that 20% of the samples evaluated below positive samples as measured per the comparator assay, meaning that the CT values are within three CT of the mean CT at the Level of Detection, or LOD, of the comparator test. Can prospective samples be supplemented with additional low positive samples, such that 20% of all positive samples in the analysis have low viral load?

Toby Lowe: Yes. We recommend that if needed, low positive samples can be supplemented with either archived samples or samples collected from convalescent patients in order to include approximately 20% low positive samples, as determined by the comparator, which right now is the FDA-cleared CDC monkeypox virus PCR-based assay.

CDR Kim Piermatteo: Thanks, Toby. Alright, our last monkeypox test development and validation question is, if a MPXV test uses Research Use Only, or RUO, instruments, such as PCR or extraction

instruments manufactured by either the test developer or another manufacturer, does FDA recommend providing a qualification protocol and For Emergency Use Only label in the tests instructions for use?

Toby Lowe: Yes. For monkeypox virus tests that use research use only instruments, the EUA template does discuss our recommendations for this. And the template discusses recommendations specifically for providing a qualification protocol, Emergency Use Only labeling or label, and quality system information, depending on whether the test developer is also the instrument manufacturer. And if a developer has specific details or situations that they need specific questions answered about, those generally are discussed as needed during the EUA review since labeling is typically finalized after completion of the substantive review of the data.

CDR Kim Piermatteo: Great. Thanks, Toby. Alright, we'll now move into our previously submitted questions about COVID-19 test development and validation. Toby, I'll be directing these questions to you again. The first question is, will FDA prioritize SARS-CoV-2 antigen test 510(k) or De Novo submissions from developers that have an existing EUA authorization ahead of developers without an EUA authorization?

Toby Lowe: Thanks, Kim. So marketing submissions, which include 510(k) and De Novo submissions, are not prioritized in the same way as EUA requests. FDA aims to review marketing submissions according to the timelines that are established under the Medical Device User Fee Amendment, or MDUFA, program. So generally, 510(k) applicants can expect submission acceptance review decisions within 15 calendar days, substantive review decisions within 60 days, and final decisions within 90 days, where these number of days are calculated as days that the submission is under FDA review-- so subtracting or not counting any dates where the submission is placed on hold due to a request for additional information from the applicant. And more information on the marketing submission process, the review process, and MDUFA timelines can be found on the FDA website.

CDR Kim Piermatteo: Thanks, Toby. Alright, our next COVID-19 test development question is, what is FDA's recommendation regarding the potential use of combined oropharyngeal and nasal self-sampling for COVID-19 rapid antigen tests?

Toby Lowe: So FDA has publicly stated that, due to safety concerns, oropharyngeal swab samples, also sometimes referred to as throat swab samples, should be collected only by a trained health care provider. Developers that might be interested in pursuing self-collection for this sample type should discuss their validation plans with FDA in advance.

CDR Kim Piermatteo: Thanks again, Toby. So our last previously submitted question today is, with the implementation of new COVID-19 test policy, is FDA also planning to implement the transition plan for medical devices that fall within enforcement policies issued during the coronavirus disease 2019, COVID-19, public health emergency soon? If so, can FDA provide an estimated implementation date?

Toby Lowe: Thanks, Kim. So we have discussed the transition plan draft guidance documents on previous town halls. And as discussed, we are working to finalize those draft guidance documents. The drafts were issued late last year. And it's important to note that those two draft guidance documents are not test specific. They're for all medical devices that fall within enforcement policies or were issued EUAs during the COVID-19 public health emergency. And they do address different situations than the newly updated COVID-19 test policy guidance.

So the draft guidance document titled “Transition Plan for Medical Devices that Fall within Enforcement Policies Issued During the COVID-19 Public Health Emergency” provides FDA's recommendations and expectations for devices under COVID-19 related enforcement policies to transition back-to-normal operations when the public health emergency expires. And it is very important to note that the COVID-19 test policy guidance is outside of the scope of that transition guidance.

And then COVID-19 tests that were issued EUAs are within the scope of the draft guidance document titled “Transition Plan for Medical Devices Issued Emergency Use Authorizations During the COVID-19 Public Health Emergency,” which addresses the transition back-to-normal operations when the emergency use declarations that allowed for FDA to issue EUAs are no longer in effect. However, we're not able to comment on estimated finalization dates for draft guidances, so we do recommend that you keep an eye on FDA's website for any updates there.

CDR Kim Piermatteo: Thanks again, Toby, for all of your responses. And thank you to those stakeholders who submitted those questions. That wraps up the previously emailed questions for both monkeypox and COVID-19 test development.

We will now take your live questions. As a reminder, 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, indicate whether the question is related to monkeypox or COVID-19, and 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.

So our first live question is coming from Dr. Farhan Khan. I have unmuted your line. Please unmute yourself and ask your question.

Dr. Farhan Khan: Hi. Can you guys hear me?

CDR Kim Piermatteo: Yes, we can.

Dr. Farhan Khan: OK. Quick question-- I haven't joined these meetings in a long while. So I just wanted to double-check if FDA is still accepting for COVID-19 EUA application, or has that stopped?

Timothy Stenzel: I'll start this response, and then I'll hand it over to Toby. But we did update the COVID guidance on September 27 with some new review priorities. And as long as somebody develops the test and it's covered under the review priorities of September 27, then we would continue to accept those applications. Toby can provide some more color to that.

Toby Lowe: Yeah. Thanks, Tim. So there is still an active 564 emergency declaration which gives us the authority to issue emergency use authorization as needed. So you are still able to submit emergency use authorization requests. And then we will evaluate them to determine whether they are something that we will prioritize.

So we do recommend, as Tim mentioned, that you take a look at the guidance that was issued on September 27 which lists out the priorities for how we intend to prioritize EUA requests and where we recommend instead using a marketing review pathway-- the traditional marketing review pathways. So take a look at that. And if you have any questions, you can send them into the mailbox. And if you

decide to, you can submit an EUA request. And we will consider it and determine whether or not we will prioritize it and let you know.

Dr. Farhan Khan: Thank you. Thank you much.

CDR Kim Piermatteo: Alright, our next question is coming from S. Grippon. I have unmuted your line. Please unmute yourself and ask your question.

Sadan Grippon: Thank you. This is Sadan Grippon from Biocrucible. This is a monkeypox question. We submitted our letter of intent for the EUA application. And we have a point-of-care assay. Therefore, we need real clinical samples for validation. And my question is, considering the difficulty in getting these samples, is it acceptable to use multiple lesion sample swabs from one subject? And if yes, how many could we take from one subject?

Timothy Stenzel: Yeah. So I think this might have been similar to a question that was previously submitted. And we didn't respond to cause we will provide questions such as this to email to developers. But we are looking for 30 unique positive samples but not in the same patient and 30 unique negative samples. Noel, I don't know if you have anything else to add to that.

Sadan Grippon: Thank you.

Noel Gerald: No, I don't have anything else to add. Thanks, Tim.

CDR Kim Piermatteo: Thanks, Tim. Alight, so we're going to go move on to our next question. Our next question is coming from Richard. Richard, I have unmuted your line. Please unmute yourself and ask your question.

Richard Montagna: Yes, thanks for taking the call. This is Richard Montagna from Rheonix. Given the decreasing numbers of monkeypox in the US, is there a threshold at which FDA would basically remove the emergency declaration and no longer accept EUAs? I know this is kind of a crystal ball question, but I just didn't want to—

Timothy Stenzel: Yeah, it's a good question. So in our government, there are at least three different determinations or declarations that the Secretary could make. And the Secretary makes these decisions. And it's our job at the FDA to initiate actions.

So we have, what, six or seven previous emergency-- EUA declarations for testing-- IVD testing-- that are still in force. So it's uncommon, and it's not time limited, these 564's, that the Secretary has to actively determine that the emergency no longer exists. And there's no longer a need for EUAs for IVD's.
And so as I said, there hasn't been one that's been discontinued in a long time. And there's a reason for that. These things, once they happen, can come back. And if a test has not been fully authorized, if we remove the 564 determination, then those tests have to come off the market at some point, unless they come in for follow-up innovation.

And an illustrative example is Ebola. So Ebola is now somewhat of concern. And we hope that the current outbreak outside the U.S. extinguishes itself very quickly and doesn't put U.S. at risk. But we're very happy that there are EUA authorized tests for Ebola that have not been required to be removed from the market.

So it's a big question. It's an important question. I don't see it happening anytime soon for monkeypox.

Richard Montagna: OK. Well, thank you very much. I appreciate the input.

CDR Kim Piermatteo: Thank you Richard, for your question. And thank you, Tim, for that response. Alright, next I'm going to call on a number, so I hope you're able to respond. I'm calling number 10357627. I have unmuted your line. Please unmute yourself and ask your question.

Yun Wynn: Yes, good morning. My name is Yun Wynn from BD. And thank you for taking my question. And it's related to SARS-CoV testing. Our at-home test includes a nasal swab. Do the nasal swabs also have to be part of the stability testing?

Timothy Stenzel: I'll turn it over to Kris. I would say in general that if the swabs are in the kit when you package the kit, it should be in that kit. And it should be part of the stability testing. But I'll let Kris verify this. And of course, you could potentially lose sterilization and other things that may impact the test performance. But Kris, do you have anything to say about that?

Kristian Roth: Yeah. Thanks, and I agree. Anytime you're going to do stability testing, you'd want to follow the instructions for use. So that would include if there is a swab, use of the swab. Typically, folks do spike a known volume onto the swab and allow that volume of sample to be completely absorbed.

And if you need some help figuring that out, we do have some folks that are on the stability team. So we can engage with you on that. But in general, yes, please include the swab and all steps in your IFU when doing stability testing.

Yun Wynn: Thank you.

CDR Kim Piermatteo: Thank you, Tim. Thank you, Kris. Alright, our next question is coming from Amanda. Amanda, I have unmuted your line. Please unmute yourself and ask your question.

Amanda: Hi, thanks for taking my question. This is regarding COVID-19 testing. So on page 11 of the pre-market validation recommendations for developers, the following is stated about reagent stability studies. So FDA considers 15 to 30 degrees Celsius to represent room temp conditions. If your test is intended for storage at room temp, evaluation of storage at 30 is generally acceptable as it represents the worst case scenario. If your device is intended for your POC or at home, the study should include storage condition of high humidity at 30 degrees.

Can you please clarify what the intent of the last comment is? Is it an additional high humidity condition on top of ambient humidity at 30 degrees? And how does FDA define high humidity? Because does this negate the need for a high humidity flex study?

Timothy Stenzel: Yeah, let me just turn it over to Kris to respond to that.

Amanda: Thanks.

Kristian Roth: Yeah. I think for the EUA, we have accepted that combined study. You can do that temperature with the humidity in parallel. Or you can do them separately as well. The intent there is to

ensure that obviously that a range of conditions that may be experienced by the kit during storage are kind of tested.

Amanda: OK. Thank you.

CDR Kim Piermatteo: Thanks, Amanda, for your question. And thanks, Kris, for the response. Our next question is coming from Wenli. Wenli, I have unmuted your line. Please unmute yourself and ask your question.

Wenli: Thank you very much. This is Wenli Jo from XYZ Laboratory. And my question is related to the COVID testing. And so for the COVID EUA application that has already been submitted and it's not on the FDA's priority list, for this type of the submission, are we supposed to-- or are we expecting to get a feedback from FDA as well?

And when would that be? How long is it going to take to hear from the FDA? And I wonder, in the feedback, does that include any review or feedback from FDA, say, if the study is good or not or what we need to do, whether it's totally rejected or suggested to transfer to the traditional market pathway? Should we wait for all those before we actually start working on the market pathway? This is a question. And yeah, important is when would we expect to hear from the FDA? Yes.

Timothy Stenzel: So I just want to clarify. You're talking about a pre-EUA submission?

Wenli: A EUA submission already submitted.

Timothy Stenzel: Oh, you submitted an EUA.

Wenli: Yeah.

Timothy Stenzel: OK. Well, we're working through all the submissions. I'm going to turn this one over to Toby to respond on this.

Toby Lowe: Sure. Thanks, Tim. So we are working our way through submissions that we've received. We are considering the priorities that are in the September 27, 2022 guidance update. And we are going through those and responding to the submitters as we are able to evaluate each submission on its merits.

So as part of that, we'll go through and look and see does the submission-- where does the submission fall, considering the new priorities that are described in the guidance, and if it is a test that we think will significantly benefit the public health. And we will respond back to each submitter. We can't give you a firm timeline for that as we are working through each of them.

And our timeline will depend on many factors specific to each submission. But we will-- you should expect to receive a response. Depending on whether we determine that we will or will not be prioritizing your submission for review will determine whether your feedback includes substantive review or just a response saying that we do not intend to prioritize review of your submission at this time.

Wenli: OK. So in this case, should we just wait until hear from your feedback before we go to the traditional market pathway? Or we can just do that simultaneously?

[INTERPOSING VOICES]

Toby Lowe: Go ahead, Tim.

Timothy Stenzel: Go ahead. No, go ahead, Toby.

Toby Lowe: OK. So as we noted in the guidance document, we are recommending that developers start moving towards pursuing marketing authorization. So there is no need to wait for feedback on your EUA request to start pursuing marketing authorization especially if you have already determined for yourself that you don't believe that your EUA request is within the priorities noted in the September guidance update.

Timothy Stenzel: OK. Thank you, Toby. We're going to go ahead and move on.

Wenli: Thank you very much.

CDR Kim Piermatteo: Thank you, Tim, and Toby. Thank you, Wenli. Alright, we're moving on to our next question, is coming from Barbara. Barbara, I've unmuted your line. Please unmute yourself and ask your question.

Barbara Ann Conway-Myers: Hello. This is Barbara Ann Conway-Myers from LumiraDx. And my question pertains to monkeypox. In the current template for sample stability, specifically section C6, it states, additional testing does not need to be performed if the specimen type is a dry swab as recommended by the CDC. However, in the summary EUA template, it also states, sample stability should be performed to shipping claims go beyond the current CDC recommendations for dry swab specimens.

So what I'm looking for is clarification. Is there no need to do stability if it's a dry swab? Because when you go to that website, the CDC also has stability shipping and storage claims for dry swabs, swabs in VTM, and lesion crusts. If we want to claim swabs in VTM or lesion crusts, do we need to perform our own stability studies rather than refer to the recommendations of the CDC?

Timothy Stenzel: I'll turn this over to Noel to respond.

Noel Gerald: OK, great. Yes. So I want to distinguish crusts from the other assistant sample types that your mentioning. But when you're considering swabs from lesions, whether their a dry swabs or swabs specifically in -- lesion swabs specifically collected in VTM, and you are not going beyond the storage and shipping conditions that are on the CDC website, then no additional validation testing is needed. For crusts, that kind of goes beyond what we are generally expecting to see in EUAs.

And so that would be something we would encourage you to discuss with us in a pre-EUA, just as a sample type in general. But if you are wanting any other transport media type or any storage claims beyond what's on that CDC site for VTM lesion swabs and dry lesion swabs, then you would want to provide validation data. I hope that's clear. Let me know if it's not.

Barbara Ann Conway-Myers: So to summarize, if I understand you correctly, as long as we are using dry swabs, swabs in VTM, or lesion crusts, as identified in the CDC supplements that were pointed to-- as long as we stay within those particular collection milieus, as well as for storage and for collection, we would not have to do any additional stability studies. It only pertains to things above what the CDC has recommended. Is that correct?

Noel Gerald: No. That's almost correct. It's the crust part. We would want to see actual validation data on crusts. Crusts kind of go beyond the scope of what we're typically seeing in these EUAs.
The template itself was mentioning just dry lesion swabs. And so really, for your question about specimen stability and shipping, if you only want to claim what's on the CDC site and not do additional validation, that's the dry swabs and the VTM only.

Barbara Ann Conway-Myers: OK.

Noel Gerald: For crusts, we would want to see some additional data. And there might be some additional discussions we would have for other validation studies. So we recommend that before going too far with crusts, that you send in a pre-EUA if that's what you really want to do.

Barbara Ann Conway-Myers: OK. Thank you so much. That really has helped us a lot. I appreciate your time.

Noel Gerald: Great. Thanks.

CDR Kim Piermatteo: Thank you, Barbara. Thank you, Noel. So our next question is coming from Ling Koh. I have unmuted your line. Please unmute yourself and ask your question.

Ling Koh: Hi, this is Ling Koh calling from BD. This is a COVID-19 question. It really is just a follow-up from one that Amanda asked earlier around the high humidity conditions for the stability study. Just wondering how high humidity conditions are defined for that 30 degree Celsius? Does the FDA have a particular percentage in mind? Thanks.

Timothy Stenzel: Kris, do you have a particular percentage in mind? I would think it would be up into the 80s and 90s.

Kristian Roth: Yeah. Yeah, thanks, Tim. You can look in the Flex Study section for what we define high humidity. But typically, I think it's 85-- 85% relative humidity.

Ling Koh: OK, perfect. Thank you so much.

CDR Kim Piermatteo: Thanks, Ling. Thanks, Kris. Alright, our next question is coming from David. David, I've unmuted your line. Please unmute yourself and ask your question.

David: Hi, this is David from MEKA Consulting. I have a question regarding the EUA of COVID-19 tests for home use. So for antigen test kits that is multiplex for COVID, flu A, and flu B, does FDA still intend to prioritize the reviewing? Thank you.

Timothy Stenzel: So I don't know. Toby, is this something that you can handle?

Toby Lowe: Yeah. Thanks, Tim. So we did discuss this on our previous town hall as well. And generally, we would suggest that those types of submissions come in for marketing authorization under the traditional marketing pathway. And we do recommend that you submit a Pre-Submission to discuss your approach there.

Timothy Stenzel: Unless, of course, after they developed it, it's sponsored by RADx, ITAP, or BARDA, or one of the other government agencies, in which case, we are under the most recent guidance update on September 27. We are continuing to prioritize government sponsored projects.

David: OK. Thank you.

CDR Kim Piermatteo: Thank you for that question, David. Alright, our next question is coming from Stacey. Stacey, I've unmuted your line. Please unmute yourself and ask your question. Stacey? Stacey, are you able to unmute?

Stacey Moltchanoff: Sorry, I thought I was unmuted. Hi, this is Stacey Moltchanoff at Thermo Fisher Scientific. Thanks for taking my question. This is related to monkeypox EUAs. Since we've passed the deadline for submission of intent to submit an EUA request, is FDA able to share how many submissions of intent have been received?

Timothy Stenzel: Can you restate your organization please?

Stacey Moltchanoff: Thermo Fisher.

Timothy Stenzel: Oh, Thermo Fisher. Oh, OK. Well, I don't think I can-- I don't think I should state the exact number. We have received quite a few, and we expect more authorizations.

Stacey Moltchanoff: Great. Thank you.

CDR Kim Piermatteo: Thank you, Tim. Thank you, Stacey. Alright, our next question is coming from Allen. Allen, I have unmuted your line. Please unmute yourself and ask your question.

Allen Chun: Yes. The pre-market validation document in the LoD Testing section, it does recommend using the most current dominant strain in circulation. So we have looked into-- this is, of course, a COVID-19 testing question. So we have looked into the most current strain available commercially. The most current available strain available commercially is BA.1 strain. Is that acceptable for LoD testing? Could you comment?

Timothy Stenzel: Kris, can you comment on that please?

Kristian Roth: Yeah, thanks. I think BA.1-- Omicron BA.1 likely would be acceptable. I'm surprised that additional strains of Omicron aren't available. If you can't find something a little bit more modern than the BA.1, just let us in that LoD Section, saying, we've looked at various locations. Just kind of establish that you've done some due diligence to try to find those additional strains. And if you have, then I think we would take the A.1. Is it an antigen test or a molecular test?

Allen Chun: It is an antigen test.

Kristian Roth: OK. OK. So I think we would probably have further discussions about what exactly antibodies you're using and the epitopes and things of that nature while we review the file.

Allen Chun: OK, great. Thank you very much.

Kristian Roth: Thank you.

CDR Kim Piermatteo: Thank you Allen, for that question. And thank you, Kris, for that response. At this time, I do not see any more raised hands. So I would like to make a call-out. If anyone has any other questions they'd like to ask our panelists today about monkeypox or COVID-19 test development and validation, please raise your hand at this time.

Alright, our next question is coming from Niya. Niya, I've unmuted your line. Please unmute yourself and ask your question.

Niya: Thank you for taking my question. This is Niya Sue from Coyote Bioscience. This question is related to monkeypox. I know we already passed the deadline. But if we have a new product and that still meet the prioritization criteria per the EUA policy, can the manufacturers still submit intent and be evaluated by FDA to see if it can fall under the EUA prioritization, or FDA would not consider any more?

Timothy Stenzel: The deadline has passed. And we do have a large number of-- amount of interest. I'm going to turn this over to Toby for a more thorough answer.

Toby Lowe: Thanks, Tim. Right, so as Tim mentioned-- excuse me-- the timeline that was noted in the guidance for when we would expect to receive the intent to submit has passed. And we did indicate in the guidance that we would generally be prioritizing review of EUA requests where we did receive that intent to submit during that time frame. However, you are able to submit an EUA request any time that there is a 564 emergency declaration in effect.

You can submit an EUA request. And we will consider it. We will consider it on the merits of the submission and considering whether the test is something that is necessary to protect the public health. But it's important to note that it would not be the type of submission that we have indicated we will intend to prioritize. So we will consider it based on the public health needs when it is submitted.

Timothy Stenzel: And I think to follow up what Toby says, to not spend resources and efforts to potentially unsuccessful end. I think it's best to go through the pre-EUA route to see if we would consider it. But even then, I'm not saying in any way that we're seeing a need to accept additional pre-EUA requests or EUA requests.

But Toby is correct, as far as the law goes. And then, of course, I want to add that the full market authorization pathway is open for orthopox and monkeypox. The CDC has a cleared test, and it would be the predicate-- the device for such a commission. And that pathway is always, always open. And we do not de-prioritize those submissions. Those submissions are decided on their own merits. And the door is always open for full authorization submissions.

Niya: Yeah. Thank you. That's very helpful. So just for my understanding, so before we put more resource on that, is it OK to communicate in a pre-EUA to see whether it would fall under the privatization?

Timothy Stenzel: Yeah. I mean, if you really want to find out, that is the most efficient route to go. But I'm not I'm not encouraging you in any way that it would be successful, given the volume of submissions that we've received so far and the state of the emergency response and the low number of positives in the United States.

Niya: Gotcha. This is very helpful. Thank you very much.

CDR Kim Piermatteo: Thank you, Niya. Thank you, everyone. Alright, our next question-- Stacy, you have another question. I've unmuted your line. Please unmute yourself and ask your question.

Stacy Moltchanoff: Hello, this is Stacy again from Thermo Fisher. I just had another question about the monkeypox template. If a product is authorized and a supplement needed to go in, would that same template that was used for the initial EUA request be required to be filled out?

Timothy Stenzel: Noel, do you have a suggestion for that? Our templates are voluntary. Use of them is voluntary. And it's up to the submitter. But Noel, do you have anything to add about that?

Noel Gerald: No. No, I don't, Tim.

Stacy Moltchanoff: Thank you.

Toby Lowe: I think--

[INTERPOSING VOICES]

Timothy Stenzel: Oh, go ahead, Toby.

Toby Lowe: Sorry. Yes. I'll just add that, as Tim said, the templates are voluntary. They are very helpful for our reviewers if you do complete them and submit your EUA request with that information. It streamlines the review quite a bit for our review staff.

And if you're needing to submit a supplement after authorization, typically you could just use the same template but only fill out the relevant portions of it. And that way it's still a format that our review staff are used to seeing, so they can find the information that they're looking for quickly and easily. But you don't need to re-complete information that we already have. You can reference your previous submission.

Timothy Stenzel: Yeah, that was perfect. And we provide them as a really helpful resource. But Toby is on point.

Stacy Moltchanoff: Great. Thank you.

CDR Kim Piermatteo: Thank you. Alright, our next question is coming from Allen. Allen, you have another question. I've unmuted your line. Please unmute yourself and ask your question.

Allen Chun: Yes, thank you. I just have another question on COVID-19. On the same pre-market validation recommendation document, it does require some randomization on several different types of

tests but not across all test requirement. Does that mean those specific test requirements are to be randomized per the document? But those tests do not specify randomization. Those are not to be randomized. Could you comment?

Timothy Stenzel: Yeah, I'm unclear on the question. Kris, do you understand the question?

Kristian Roth: Not really. I mean, there's a number of studies, both pathogen and molecular, point-of-care, high complexity, over-the-counter. And so I think where we've mentioned randomization, that is where we recommend randomization be employed. I think some studies maybe don't have that. And in those situations, we didn't mention randomization.

Allen Chun: Right. So my question is, those tests that do not mention randomization, does that mean those tests do not require randomization? So that's my follow-up question.

Kristian Roth: Likely, yes. I guess if you have a specific question about a specific study, you can send that into the templates-- or sorry, the COVID DX email inbox. And that's likely a better source of an answer rather than something general that we'd say here.

Allen Chun: Yeah. So for example, we already conducted shelf-life stability testing. And shelf-life stability testing would not have been randomized. So that'll be my very specific question.

Kristian Roth: Sure. And if randomization is not mentioned in that section, then I think we would accept a non-randomized study for that shelf-life stability.

Allen Chun: OK. Great. Thank you.

CDR Kim Piermatteo: Thank you Allen for that question. And thank you Kris for that response.

Alright, at this time I will move to close today's town hall. I want to thank everyone for your participation today. And again, I want to thank our panelists, Tim, Toby, Kris, and Noel, for providing their responses.

So today's Virtual Town Hall presentation and transcript will be posted to CDRH Learn under that new section titled In Vitro Diagnostics, and then the subsection titled Virtual Town Hall Series.

For specific questions about monkeypox test development, you may send an email to MPXDx@fda.hhs.gov. And for specific questions about COVID-19 diagnostic development, you may send an email to COVID19DX@fda.hhs.gov.

As a reminder, our next Virtual Town Hall, which will be for monkeypox test developers specifically, is on Wednesday, November 9, 2022 from 12:05 to 1:00 PM Eastern time. I hope you can join us again.

This concludes today's Virtual Town Hall. Have a wonderful day.

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