

CDRH Virtual Town Hall #95
Monkeypox Test Development and Validation
October 12, 2022

CDR Kim Piermatteo: Hello and welcome to today's Virtual Town Hall number 95 for monkeypox test developers. Today we will discuss and answer your questions about diagnostic tests in response to the monkeypox public health emergency.

Thanks for joining us today. This is CDR 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.

Dr. Timothy Stenzel is on leave this week. Our panelists for today are Toby Lowe, Associate Director for Regulatory Programs in 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 Toby is Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices also 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 questions about monkeypox. And then lastly, we will address your live questions. The presentation and transcript for last week's monkeypox Virtual Town Hall were posted this morning. So please take a look at those.

And the following Virtual Town Hall dates provided on this slide have been confirmed. They are October 26, November 9, and November 30, all at the same time as today. Please mark your calendars. 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" web page for details on all upcoming Virtual Town Halls. Links to both of these web pages have been provided on this slide.

And lastly, as a friendly reminder, for those of you participating live in today's town hall, please be sure you've joined the town hall via the Zoom app and not through a web browser to avoid any technical issues.

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

Toby Lowe: Thanks, Kim. Thanks everyone for joining us yet again for another town hall. So a couple of quick announcements. First, last week, we did authorize the first commercial test kit, authorized under EUA for detection of monkeypox. That is the Abbott Alinity m MPXV, excuse me, test, which is our real time PCR test for the detection of monkeypox DNA using lesion swab specimens from individuals suspected of monkeypox virus infection. And that is authorized for use in moderate and high complexity laboratories.

So we also wanted to give another reminder. Kim, I think on the next slide? Thanks. Of October 13, which is tomorrow, that is 30 days after the publication of the notice of availability of the monkeypox test policy guidance. And so that is the deadline that we've noted in the guidance for laboratories to notify FDA of their LDTs that they are using for monkeypox as well as the deadline for experienced developers to inform FDA by email of their intent to submit an EUA request for a monkeypox diagnostic

test. So if you are one of those entities and have a notification or an intent to submit, please make sure to send that into FDA to the MPXDx mailbox noted at the bottom of the slide by tomorrow.

And then sort of along the lines of those notifications from laboratories, we want to again remind callers that the FDA generally does not expect an EUA request for certain types of validated monkeypox diagnostic LDTs. And those are the tests that are developed and performed in a single site high-complexity CLIA-certified laboratory and use PCR and lesion swab samples.

Under the policy in the current monkeypox policy guidance, we expect a notification by email by tomorrow. Without any data, we don't intend to review data or provide a decision on an application. And we don't intend to issue an EUA. We just want to see that notification. And outside of a declared emergency, as well as prior to the declared emergency for monkeypox, we generally have exercised enforcement discretion for LDTs, and for this subset of monkeypox diagnostic LDTs, we have also implemented a narrow policy of enforcement discretion after the EUA test declaration for monkeypox.

So with that, I think we can move on to questions.

CDR Kim Piermatteo: Great. Thank you, Toby, for those remarks. We will now answer your previously emailed questions. 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 town hall. For those questions, we will try to send a response in writing within a few days. If you have received, or 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 for an update.

So Toby, I'll be asking you one previously emailed question today. That question is, is IRB review and approval required for analytical studies that use contrived samples?

Toby Lowe: Thanks, Kim. So generally, studies that involve human specimens conducted in support of an EUA request are subject to applicable Institutional Review Board, or IRB, review and approval, and informed consent. This information about this can be found in 21 CFR parts 50, 56, and 812. And there's also information in the monkeypox EUA template about this.

And there may be some protections in place in the situation described in this question, such as informed consent and IRB approved collection protocols for human samples that are purchased from a commercial vendor such as the human samples that may be used to create the contrived samples used in these studies. So if you have questions regarding whether your specific studies require IRB review and approval, we recommend that you consult with your IRB.

CDR Kim Piermatteo: Thanks, Toby. Alright, that wraps up the previously submitted questions for monkeypox today. So we will now move to take your live questions. 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. 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 it looks like our first question is coming from Richard. Richard, I have unmuted your line. Please unmute yourself and ask your question.

Richard Montagna: Yeah, thank you for taking the call. This is Richard Montagna from Rheonix. I have a question about the deadline for submitting either the letter of intent or for a CLIA lab. We submitted our letter of intent for an EUA about two weeks ago and haven't heard anything yet. And we just didn't know if you're just waiting until October 13 to respond to everyone. Or should we have expected a response?

And related to that, we also operate a New York State licensed CLIA laboratory that does intend to offer monkeypox tests. And we interpreted the guidance as we need to notify you within five days of starting to offer that. But I thought I heard you say this morning, we still have to let you know by October 13 that the CLIA lab intends to offer an LDT. So if you could clarify that, I'd appreciate it. Thanks.

Toby Lowe: Thanks. So let me start with your first question and then make sure I followed your second question. So your first question about your intent to submit, we are working on those. And you will get a response. Don't need to worry about not having gotten a response yet. For some of those, we need to see sort of all of the intent to submits that we get in and evaluate them, the priorities as a whole.

Richard Montagna: OK, thank you.

Toby Lowe: And then I believe your second question was about the laboratory notifications and whether the five days of, or within five days of offering went beyond the 30 days. Is that what the question was there?

Richard Montagna: Well, I guess we-- the lab is not ready to offer the test yet. But they assumed that once they got certified through New York State that-- and started offering, we would have five days to let you know that we were doing that. Is that true? Or do we have to let you know by October 13, tomorrow, that we do intend to eventually offer an LDT through our CLIA lab?

Toby Lowe: Yeah, so we do note in the guidance that we intend to accept notifications for 30 days after publication of the notice of availability of the guidance. So we do expect to receive any such notifications by tomorrow, and if the laboratory is intending to offer that test.

Richard Montagna: OK, thank you very much. I appreciate it.

CDR Kim Piermatteo: Thank you, Richard. Thank you, Toby. So our next question is coming from Niya. Niya, I've unmuted your line. Please unmute yourself and ask your question.

Niya Su: Oh, thank you for taking my question. This is Niya Sue from Coyote Bioscience. I have a question regarding the chemical evaluation with contrived samples. Can we use genomic DNA to spike into the natural negative chemical matrix instead of using the inactivated virus?

Toby Lowe: Noel or Kris, do you want to address this one?

Noel Gerald: Sure. I can take this one. Yes. So genomic DNA is one option that's currently accepted. There's a list of materials that you can see on our FAQ page that you can spike, considering also that it meets the other recommendations in the template for individually unique clinical specimens that you're spiking into.

Niya Su: Got you, thank you very much.

CDR Kim Piermatteo: Thank you, Noel. Our next question is coming from Landon. Landon, I have unmuted your line. Please unmute yourself and ask your question.

Landon Stovall: This is Landon Stovall from [INAUDIBLE] lab in New York City. My question was about the stability experiments. Would we need to perform the stability experiment if we are going to match the CDC's guidelines of up to seven days?

Noel Gerald: OK, just to make—

Toby Lowe: Go ahead, Noel. Go ahead, Noel. Uh-oh. Noel, did we lose you?

Kristian Roth: We may have lost Noel. I think the general answer is—

Noel Gerald: Can you hear me?

Kristian Roth: There we are. Noel you're back. Yes?

Noel Gerald: Yes. Yes, sorry. So just to confirm, this is specimen stability for a nucleic acid base test?

Landon Stovall: Correct.

Noel Gerald: And then your question is, if you're just going to use specimen stability recommendations that are consistent with what CDC has posted online, do you need to do separate specimen stability validation testing?

Landon Stovall: Correct.

Noel Gerald: No. So if you are using dry swabs or VTM as described on the CDC website, and you're going to be completely within what's posted there, then we will not require to see specimen stability validation from you to support your EUA.

Landon Stovall: Thank you so much.

Noel Gerald: Sure.

CDR Kim Piermatteo: Great. Thank you very much, Landon, for that question. Alright, our next question is coming from Sumrita. Sumrita, I have unmuted your line. Please unmute yourself and ask your question.

Sumrita Bhat: Hi everybody. This is Sumrita and I'm here, I'm quality and compliance director at Cardiai Labs. Our lab is located in Calgary, Canada. So I think my question would be a little bit different from other questions that people from CLIA Lab are asking. Our lab is accredited at the provincial level. And our research group has actually conducted lots of studies, in silico studies, for monkeypox. But we are having a major limitation with getting the clinical sample.

So I have two questions here. So first question would be, can FDA suggest any resource for getting the monkeypox clinical samples? And the second question would be, can we submit only the in-silico

validation? And third question would be related to the previous question that I think Leanne asked about, is there a way that we can spike a synthetic nucleic acid into a nasal-- into a similar matrix like a negative nasal matrix, or a reconstituted matrix that can be used to support the validation?

Toby Lowe: Thank you. So that's-- there's a lot of moving parts there in your question. So I think that may be best to send that into the mailbox so that we can take a look through all the different pieces and get some appropriate recommendations back to you.

Sumrita Bhat: Yeah, I have already sent this question before the webinar. So I hope I can get an answer for that as soon as you guys can.

Toby Lowe: OK, great. We will-- we'll make sure someone gets back to you.

Sumrita Bhat: Thank you so much.

CDR Kim Piermatteo: OK, thank you, Toby. Alright, our next question is coming from Lynne. Lynne, I have unmuted your line. Please unmute yourself and ask your question.

Lynne Doucette-Stamm: Great. Thanks for taking my question. This is a follow up to the earlier question about an LDT, LDT being developed in a CLIA lab. It was our understanding that to file by-- to send the email by tomorrow, it had to be fully validated, our assay. Can it still be in development and we can send the email tomorrow and then notify you five days after that within five days of offering it?

Toby Lowe: Thanks for that question. So excuse me. The language and the guidance does say that the tests should be fully validated. And that is the preferred scenario and the sort of appropriate use of the policy. If your test is almost validated or you are working on finishing that, that's something that we can consider. But ideally, yes, the test should be fully validated and notified by tomorrow.

Lynne Doucette-Stamm: OK, thank you very much.

CDR Kim Piermatteo: Thank you Lynne for that question. Alright, Niya, it looks like you have another question. I've unmuted your line. Please unmute yourself and ask your question.

Niya Su: Thank you. So the question I have is for the first EUA authorized commercial kit from Abbott, does FDA consider that as a qualified EUA comparator in the clinical evaluation?

Noel Gerald: I can take that one.

Toby Lowe: Go ahead. Yep, no.

Noel Gerald: Unless you want to Toby.

Toby Lowe: Yeah, no.

Noel Gerald: Your question is can the recently authorized Abbott tests be used as the comparator test for your clinical validation studies for your candidate test? Is that correct?

Niya Su: Correct.

Noel Gerald: Not at this time. So we would want it to be a sensitive test that has been established with real natural clinical samples. And for the initial authorization, the validation data was only provided so far with contrived clinical samples. So at this time, it would not be an acceptable comparator.

Niya Su: Gotcha. Just to confirm my understanding in terms of evaluating qualified comparator, the comparator must have completed the clinical evaluation with the natural clinical samples, not just the contrived sample. Is that right?

Noel Gerald: Yes. That's how we base our assessment that it's sensitive. It's sensitive with a clinical sample evaluation, not just contrived.

Niya Su: Gotcha. OK, thank you.

Noel Gerald: Sure.

CDR Kim Piermatteo: Thank you, Niya, for that question. And thank you, Noel, for that response. Our next question is coming from Wenli. Wenli, I've unmuted your line. Please unmute yourself and ask your question.

Wenli: Thank you very much for accepting my question here. This is Wenli Cho from XYZ Laboratory. And I just have a question. I know [INAUDIBLE] FDA is very busy reviewing all those notifications. I'm just wondering if there's any quota on the number of EUA requests that will be accepted or as much as that notification that meets the FDA's priority requirements that will be granted the EUA requests. I'm just wondering if you could give me some input on this. Thank you.

Toby Lowe: Yeah. So no. Sorry. There's-- if I'm understanding your question correctly, we are evaluating the submissions that come in. And we will consider each one for whether it meets the priorities.

Wenli: Hello?

CDR Kim Piermatteo: OK, thank you. Yes, I hear you, Wenli.

Wenli: I'm sorry. Yeah. My mic [INAUDIBLE]. It's not working now. So, OK.

CDR Kim Piermatteo: OK, Wenli. You're all good. OK? We're going to-- OK, we're going to move on to our next question. Our next question is coming from Sumrita again. I've unmuted your line. Please unmute yourself and ask your question.

Sumrita Bhat: Thanks a lot for taking my second question. Really appreciate it. I have a question regarding the comparator method that we just discussed that clinically proven, like the comparator should have a clinical-- should be tested with clinical samples and not contrived. I was just wondering, does FDA has any kind of a recommendation? Because I remember when we initially started COVID, we had a couple of tests from Roche and other companies. Those were considered as a gold standard. Is there anything like that here, which can make our things easy? Any recommendation would be appreciated.

Toby Lowe: So I believe we've discussed previously on the town hall that right now, we are-- we've generally recommended using contrived specimens for validation. And that is-- that's all discussed in detail in the EUA template that's on our website. In terms of comparators, if you wanted to use clinical specimens instead of contrived, right now, the CDC cleared assay is the only appropriate cleared or approved or, sorry, cleared or authorized comparator.

But that generally only works if there is-- if you're able to get leftover specimens as well as the results from using the CDC assay from a laboratory that's already using that assay for clinical use.

Sumrita Bhat: Yeah, thank you so much for that.

CDR Kim Piermatteo: Thank you, Sumrita, for that question. And thanks, Toby, for that response. Alright, at this time, I would like to make a call out for anyone who has any more questions for our panelists today. Please raise your hand.

OK, seeing none. We will go ahead and move to close today's town hall. I would like to thank everyone again for your participation today. And again, I want to thank our panelists Toby, Kris, and Noel.

So today's Virtual Town Hall presentation and transcript will be posted to the FDA web page titled "Virtual Town Hall Series - Test Development and Validation During Public Health Emergencies for Monkeypox and COVID-19" webpage under the section "Previous Town Halls for Test Development and Validation During Public Health Emergencies."

For specific questions about monkeypox diagnostic development, you may send an email to MPXDx@fda.hhs.gov.

I hope you're able to join us again for the next Virtual Town Hall, which will be for both monkeypox and COVID test developers on Wednesday, October 26th, 2022 from 12:05 to 1:00 PM Eastern time.

Thank you again for joining us. This concludes today's Virtual Town Hall. Have a wonderful day.

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