CDRH Webinar: Policy for Monkeypox Tests
September 14, 2022

Moderator: CDR Kimberly Piermatteo

CDR Kim Piermatteo: Again, welcome. Thank you 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 webinar.

Our topic for today is the final guidance titled "Policy for Monkeypox Tests to Address the Public Health Emergency," which the FDA issued last week on September 7th. We're holding today's webinar to provide you with an opportunity to learn more and to answer questions you may have about this final guidance, and monkeypox test development and validation.

Our panelists for today's webinar 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 OHT 7, in CDRH's Office of Product Evaluation and Quality, or OPEQ. Joining Tim is Toby Lowe, Associate Director for Regulatory Programs in OHT 7, and Dr. Kristian Roth, Deputy Director of the Division of Microbiology Devices, also in OHT 7.

We'll begin with a brief introduction today from Tim, followed by a presentation from Toby. And then we will address some previously submitted questions. And lastly, we will field your live questions.

Before I turn it over to Tim, I'd like to remind our attendees today that we recommend you join today's webinar via the Zoom app and not through a web browser to avoid any technical issues. Thank you all again for joining us today. Tim, the floor is now yours.

Timothy Stenzel: Thank you, Kim. And welcome, everyone, to this first webinar or town hall on monkeypox tests. We will hold these monkeypox calls weekly as we monitor, of course, attendance of the calls and the need for a weekly cadence and make updates to the schedule at a later date.

As for COVID, we are-- rather, as for monkeypox, we are here to inform and answer pre-submitted questions followed by a live question format, as we did for COVID. But today, after I give my introductory remarks, Toby will present slides to inform and to discuss the recent declaration for tests, guidance and the template, before we move on to questions that have been submitted prior to this call, and then to live questions.

We will continue to take COVID questions once a week-once a month, rather. And we'll have a combined COVID-monkeypox call. And the next COVID call which will be combined with monkeypox will be on September 28th. So we ask that you hold your COVID questions till then. Or you can always email our COVID email box.

We are working on a template for monkeypox rapid antigen tests and are encouraging interested developers to apply to the NIH monkeypox ITAP program, which NIH has announced last week and has already begun accepting applications.

As we have stated in other forums previously, where monkeypox, contrived samples are acceptable if natural samples are not available. However, this is only recommended for lesion swab samples for molecular tests. In particular, antigen tests will need to have actual patient samples in order to assess their performance.

The FDA has begun bioinformatic analysis of published monkeypox sequences in order to determine the impact or potential impact on tests, including the CDC, FDA-cleared NVO test that is currently being used in the LRN labs and in five major reference labs. We expect test developers to do the same for their test. That is, evaluate for any mutations. There is a reported deletion in the TNF receptor gene that has knocked out testing. There was only three patients where this happened. But it has caused false positives in apparently only three patients. However, we do recommend that test developers design around this region of the monkeypox virus in order to avoid false negatives.

We encourage more than one target for molecular assays to reduce the risk of false negatives. And finally, where the technology allows, we recommend that a sample collection adequacy control be included in tests, as we have seen up to a 15% sample collection inadequacy rate so far in the response that, in those cases, did require re-testing. So it's important to know when the sample is inadequate because this would protect against the risk of false negatives.

It does appear that the lesions in these cases were not adequately swabbed, as everything else has been eliminated to our knowledge as a source of those potential false negatives. So these controls are important. With justification, the FDA will consider authorizing tests without a sample collection adequacy control, and will consider a post-market commitment to add such a control after authorization.

OK. That does conclude my introductory remarks. Kim, I guess it's time to have Toby go ahead and present.

CDR Kim Piermatteo: Great. Thanks, Tim. Toby, I'll go ahead and turn it over to you now for your presentation.

Toby Lowe: Thanks, Kim and Tim. So I think we can get started on the next slide. Thanks, everyone, for joining us. We wanted to start out by talking through some of the actions that were taken on September 7th, specifically starting with the HHS Secretary issuing a 564 declaration for the emergency use of IVDs for monkeypox. That announcement essentially opened the door to our ability to accept EUA requests.

Following that declaration, we issued a guidance document, the “Policy for Monkeypox Tests to Address the Public Health Emergency.” And then that same day, we also issued the first monkeypox emergency use authorization. So we will talk through those actions in a little bit more detail as we go through this presentation. So we can move on to the next slide.

This slide mostly just has information that we hope will be beneficial to you all as monkeypox test developers. As part of the guidance document that we issued, we also put out templates. So the link for those templates is included here. And as Tim mentioned, we will continue to work on adding more. We also put up a new web page with frequently asked questions on testing for monkeypox. I suspect most of you are familiar with our FAQ page for COVID. That has been very popular through the past couple of years, so we used a similar format for monkeypox.

And then there's the link for the virtual town halls and today's webinar with the email address and questions in advance, and all of the information about future town halls, as well as these slides, and transcripts, and everything will be posted on that web page. And then, of course, the monkeypox email address, MPXDx@fda.hhs.gov is where you can send any questions, as well as your pre-EUA and EUA submissions.

So going to the next slide, we can start talking through the content of the guidance document. So the guidance document is titled "Policy for Monkeypox Tests to Address the Public Health Emergency." And it goes through a few different points. First, it starts out with outlining FDA's review priorities for emergency use authorization requests for monkeypox diagnostic tests.

Then, it also includes enforcement policies for certain diagnostic tests developed and performed by single-site high-complexity CLIA labs, recommendations for test validation, enforcement policies for modifications to cleared or authorized monkeypox diagnostic tests, and enforcement policies for certain serology tests. So, moving to the next slide.

The review priorities for EUA requests will focus on particular areas, specifically for diagnostic tests. We'll focus on high-throughput diagnostic tests, tests with home specimen collection, and rapid diagnostic tests. And for all of these, we're looking for EUA requests from experienced developers with a high manufacturing capacity that inform FDA within 30 days of the guidance of their intent to submit an EUA request.

So that is a new concept that we've added here in this guidance, where we are asking that developers send in some information ahead of time so that we can prioritize our workload and also provide as much information as early as possible back to the developers so that you know right away whether or not we intend to prioritize review of your EUA request. So, going to the next slide.

We can go through an overview of the policies that would impact laboratories that are developing monkeypox diagnostic tests. Generally, we are not expecting EUA requests for certain monkeypox diagnostic tests, when the laboratory notifies FDA, and when the test meets certain specific test qualities that are noted here. So those are developed and performed in a single site, CLIA-certified, high complexity laboratory.

We're looking at molecular PCR tests here that use lesion swab samples and that are appropriately validated. We're asking for those notifications to be within five business days of offering the test, or for tests that were already offered prior to the date of the guidance, within five business days of the date of that guidance. And as of right now, we're intending to accept notifications for 30 days after the publication of the guidance.

And we will monitor the situation. And we may adjust as needed, which may include shortening or lengthening that time period of when we will be accepting those notifications. And then, for modifications, the guidance spells out certain validated modifications to a cleared or authorized monkeypox diagnostic test where we will not expect EUA requests with notification to FDA.

OK. So moving to the next slide, we will now go through the overview for commercial manufacturers of monkeypox diagnostic tests. So generally, we do expect developers to submit an EUA request or a premarket submission and receive authorization or clearance, through a 510(k), prior to offering or distributing a monkeypox test.

As I mentioned earlier, we're asking that you inform FDA within 30 days of the guidance of your intent to submit an EUA request. And those can be sent to the monkeypox diagnostics email address.

We also do not intend to object to implementation of certain modifications-- and those are outlined in the guidance-- to a developer's own cleared or authorized monkeypox diagnostic test while we conduct our review. So that's after the developer submits a supplemental EUA request or premarket submission. And while we review that, the developer can implement that modification, and FDA does not intend to object to that. So, to the next slide.

As I mentioned in the intro, we did issue voluntary templates. There are two that are currently posted. There's an EUA summary template for developers of molecular diagnostic tests for monkeypox, and that's a higher level summary that provides sort of the top level information of what we're looking for validation. And then the second one, the EUA template for developers is more in line with the level of detail that you might be familiar with from the COVID templates.

These are voluntary. We recommend that developers use them, as they do provide our recommendations for validation of monkeypox diagnostic tests. And similar to how we did or how we have been doing throughout COVID, we do intend to update the recommendations as appropriate throughout the outbreak.

Next slide talks about monkeypox serology tests. It's important to note, as discussed in the guidance, that these are not used to diagnose or aid the diagnosis of an active infection. They're not tests of immunity, and they generally may be used to further our understanding of the disease process.

So to that end, at this point, we do not intend to object to the use of monkeypox serology tests that are developed and performed in a high-complexity, CLIA-certified lab that is part of an entity that conducts research on diseases and is integrated into the direct medical care of the patient.

So typically, these are referred to as academic medical centers. And we are asking that the laboratory notify FDA of validation. And the guidance lays out certain information that we recommend be included in the test reports for those tests.

So moving onto the next slide, the last--excuse me. The last action that we took as part of that September 7th package or actions on that day was issuance of the first monkeypox EUA. So this was to Quest Diagnostics for their monkeypox virus qualitative real-time PCR that is intended to detect monkeypox and other non-variola orthopoxvirus. And it also uses lesion swab specimens. So that was issued on September 7th, along with the guidance and the other actions.

Moving to the last slide of the presentation. It has links as resources for everyone. And with that, I think we can move into the questions that we prepared that were submitted ahead of time.

CDR Kim Piermatteo: Thank you, Toby, for that presentation. We'll now answer, as Toby mentioned, a few previously submitted questions. 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, you may reach back out to the MPXDx@fda.hhs.gov mailbox for an update.

So Toby, I'll be directing these questions to you. And the first question is, "It sufficient to demonstrate cross-reactivity-- also known as analytical specificity-- where we demonstrate the specificity of our primers and probes in the presence of a mix of non-variola orthopoxviruses?"

Toby Lowe: Thanks, Kim. So as we do state in the guidance, our initial validation recommendations are for clinical validation with contrived specimens. But if clinical samples become more widely available, we may revise that recommendation. We do not consider analytical validation alone to be sufficient.

And for additional information, we recommend that you refer to the templates for EUA submissions. And they are available on the web page. That is-- let's see. The second bullet I think there is the EUA authorization page that's shown on this slide.

Timothy Stenzel: Yeah. Thanks, Toby. This is Tim. So I would add that, for the contrived samples, we're recommending that only for a lesion swab samples for molecular tests, as that is a sample type that we're very familiar with due to the CDC-cleared assay for monkeypox. Thanks, Toby.

Toby Lowe: Thanks, Tim.

CDR Kim Piermatteo: Great. Thanks, Tim and Toby. Toby, our next question has two parts. I'll read the first part, and let you answer that, and then we'll go to the second part. So the first part is, what are the current clinical evaluation recommendations for molecular diagnostic tests, especially if we do not have access to positive samples for validation?

Toby Lowe: Sure. So this is similar to the previous answer. We'll go into a little more detail, as noted in the templates. At this time, we do have the initial validation recommendations for clinical evaluation with contrived specimens. And as Tim noted, this is for lesion swab samples for molecular tests.

And we may revise that recommendation if clinical samples become more widely available. So if no natural clinical specimens are available at the time of your validation, we recommend that fully contrived specimens be used for clinical evaluation to support an initial authorization, and that they be prepared using a unique, natural clinical specimen matrix. For example, human skin lesion material specimens are spiked with quantified material to create the contrived specimen.

As noted before, this is only recommended for lesion swab samples for molecular tests. And there's more information in the EUA templates on clinical study design recommendations.

So when preparing those contrived specimens, we recommend spiking quantified virus. For example, live virus are inactivated via heat treatment, chemically modified, or irradiated, or genomic DNA, or synthetic DNA until there are viral isolates of the currently circulating strains available.

And so those would be spiked into natural clinical matrix, which would be human skin lesion material specimens. And if you are using those contrived specimens, we would recommend that you take a look at our FAQ page, where there is a list of appropriate test materials for validation.

CDR Kim Piermatteo: Thanks, Toby. All right. The second part to that question is, "If the primers and probes used in our real-time PCR detection kit are identical to the FDA-cleared CDC test, what are the validation recommendations?

Toby Lowe: Thanks. So this is also discussed in the guidance. And as discussed there, to show validation for tests developed using primers and probes that are identical to the FDA-cleared CDC non-variola orthopoxvirus test, we generally recommend that an evaluation of the limit of detection, or LOD, and a clinical agreement study demonstrate adequate performance.

Inclusivity and exclusivity testing is not recommended, as that has been done for the cleared assay. And as Tim discussed earlier, the FDA will continue to monitor the mutation status of monkeypox and the impacts on the cleared test. And for additional information on the recommendations for the performance evaluations, you can take a look at the voluntary templates on the website.

CDR Kim Piermatteo: Great. Thanks again, Toby.

All right. Our next question is, if we do have access to positive clinical samples, can FDA clarify how test developers can obtain the FDA-cleared CDC non-variola orthopoxvirus test from the CDC for use as a comparator test?

Toby Lowe: Yeah. Thanks, Kim. So as stated in the guidance and as we've mentioned, our initial validation recommendations are for clinical validation with contrived specimens for molecular tests using lesion swab samples. But if clinical samples become more widely available, we may revise that. And we know that some developers do have access to clinical samples. So if you do, we recommend a clinical agreement study with at least 30 positive and 30 negative samples evaluated by both a candidate test and a comparator test.

We recommend using a high-sensitivity FDA-cleared or EUA-authorized RT-PCR assay, which uses a chemical lysis step followed by solid phase extraction of nucleic acid such as silica bead extraction as the comparator test. If you have questions about choosing an appropriate comparator or are having difficulties accessing comparator testing, you can reach out to us at MPXDx@fda.hhs.gov.

And regarding the CDC tests, only laboratories that are designated by the CDC, which includes their LRN, the Laboratory Response Network, and five additional laboratories at this point. Only those designated labs may perform the FDA-cleared CDC test. Those labs may provide leftover samples that other developers can use for validation. And when doing so, they can provide the CDC test results, along with the cycle threshold, or Ct, values observed for each sample upon request.

If you've acquired positive clinical samples elsewhere, you may consider reaching out to one of the laboratories performing the FDA-cleared CDC test to determine if they're able to run those samples for you. And again, if you have difficulty accessing comparator testing, please reach out through the Email box.

Timothy Stenzel: Thanks. Just to just add a clarifying comment about the CDC, the FDA-cleared CDC test, and the labs that run it. So the FDA has allowed, authorized, the CDC to designate the labs that can run the test. So that is not an FDA decision on which labs run the CDC tests. Thanks. Back over to you, Toby.

CDR Kim Piermatteo: Great. Thanks, Tim and Toby.

All right. Our next question is pretty long, so bear with me. It is, "Per the FDA template for developers of molecular diagnostic tests for monkeypox, the Clinical Evaluation section describes that if fewer than 20% of positive samples are low-positives, per the comparator assay, the prospective samples should be

supplemented with additional low-positive samples. As the CDC is not releasing the cycle threshold data to the laboratories that share leftover specimens, can qualitative comparison data be submitted alone to fulfill the clinical validation portion of the EUA submission?"

Toby Lowe: Thanks, Kim. So laboratories that are designated by CDC to run the cleared CDC test may provide leftover samples that other developers can use for validation, as we mentioned. And those laboratories should provide the CDC test results, along with the cycle threshold, Ct value observed for each sample upon request. It is the average Ct values from the LOD study that are not published for the CDC test. And so we recommend that you reach out to FDA by email to MPXDx@fda.hhs.gov for feedback on the percentage of low-positive samples in your data set.

In your email, you can include the Ct values for each result in an Excel format, and also note the specific RT-PCR instrument and extraction platform configuration that were used to generate the results with the CDC test. And as we've mentioned before, and in the EUA templates, contrived samples are only recommended for lesion swabs for molecular tests if clinical samples are not available.

CDR Kim Piermatteo: Thanks, Toby. All right. So our next previously submitted question is, "Can a transport media that received an emergency use authorization for COVID-19 be used to transport suspect monkeypox samples?"

Toby Lowe: So FDA has not issued an EUAs for transport media. That's true for COVID-19 or for monkeypox. We did issue a guidance document titled “Enforcement Policy for Viral Transport Media During the COVID-19 Public Health Emergency” that provides regulatory flexibility for certain types of transport media to address potential shortages during the COVID-19 public health emergency. And developers of monkeypox tests that are intended for use with transport media should validate their test for use with that transport media, including validation of each claimed transport media in analytical and clinical studies.

We at the FDA will monitor the transport media supply situation for monkeypox and, if needed, we will address that issue. You can also reference the CDC website titled “Collection, Storage, and Shipment of Specimens for Monkeypox Diagnosis.” And if using transport media, that website might be helpful. And noting that only VTM is accepted at CDC at this time, and they're not recommending to use universal or other transport media.

CDR Kim Piermatteo: Thanks, Toby. Our next previously submitted question is, "Can FDA clarify the minimum number of tests per instrument per day that is considered high throughput?"

Toby Lowe: As we stated in the guidance document, we do intend to prioritize review of the EUA requests of high throughput diagnostic tests from experienced developers with high manufacturing capacity where authorization would significantly increase testing capacity to address public health needs.

Since the throughput of the test is one of several factors considered for prioritization, and as noted in the guidance, we recommend that developers send information, including the test throughput manufacturing capacity and other information as discussed in the guidance, to FDA indicating their intent to submit an EUA request for a monkeypox diagnostic test.

And then, FDA intends to respond to those emails, noting whether we intend to prioritize review of the proposed test at that time. That information can be sent to MPXDx@fda.hhs.gov using the subject line Diagnostic Test for Monkeypox-- Intent to Submit the EUA Request Test Summary Information.

CDR Kim Piermatteo: Thanks for that response, Toby. All right, our last previously submitted question is, "Why are monkeypox serology tests limited to CLIA-certified academic medical center laboratories?

Toby Lowe: So as discussed in the Policy for Monkeypox Tests to Address the Public Health Emergency, the guidance document, FDA has limited the scope of monkeypox serology tests to high-complexity CLIA-certified academic medical center laboratories as a way to mitigate the potential misuse of serology test results, while also fostering research from availability of data from serology testing of patients.

Currently, monkeypox serology tests cannot be used to diagnose or aid in the diagnosis of an active infection, and they are not tests of immunity. Therefore, it is important that results from monkeypox serology tests be used for appropriate purposes and that the results be properly communicated.

As discussed in the guidance, academic laboratories can test their patients daily or frequently over a period of time to monitor immune response, and are most likely to benefit from the information learned from serology testing at this stage of the monkeypox outbreak. And it's important to note that the traditional marketing submission pathway is available for serology tests.

CDR Kim Piermatteo: Thanks again, Toby. So that wraps up our previously-submitted questions. We will now move to take your live questions. As a reminder for those, 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 another reminder is we will not be taking COVID questions today. So please hold those for the next COVID and monkeypox combined webinar.

And so we will move to take our first live question, which is coming from Eugene. Eugene, I have unmuted your line. Please unmute yourself and ask your question.

Eugean Jiwanmall: So thank you, thank you, Kimberly. My name is Eugean Jiwanmall. I'm from Independence Blue Cross's Medical Policy and Technology Evaluation Team in Philadelphia. I just want to clarify that for other than high throughput, rapid testing, and home specimens, the EUAs are not required. However, FDA has outlined, if we read it and go by this presentation, what the validation of those tests should look like when they're submitted in five days parameters that are there. Is that correct that EUAs not required for those? However they should be informing FDA as has been discussed in the guidance and this presentation. And then for serology, is it correct to assume that those are purely for research purposes at this time?

Timothy Stenzel: So I'll take the second question first. So we are allowing enforcement discretion for the prescribed labs in the guidance, which typically correlate with academic medical centers to perform serology testing. The FDA's purview is not around reimbursement. We do state that serology testing should not be used for diagnosis, and at this point, FDA is not ready to say that it won't be useful for

patients who have monkeypox. So I think that's a question that's really outside of the FDA's lanes, but I want to be very clear on FDA's position. I will follow up on that.

And let me go back to your first question. I think it was about LDT tests and does it require an FDA submission and-- and/or authorization, and what are the recommendations for validation? So first, as the guidance defines an LDT, laboratory developed test, is a test that's designed, developed, validated and offered in a single site, CLIA high complexity lab. And so anything that's outside of that-- so multiple sites, anything involving self-collection or home collection, on-site, outside an academic center, or-- and that's also-- it only applies to lesion swabs.

So any non-conventional sample, we encourage those labs or any developer to reach out to the FDA if they're interested in another sample type than swabs. That's the swab-- that's the lesion-- that's the sample type that we have the most experience with and is performing well in the current outbreak. And we want to make sure that the testing is as good as it can be for monkeypox, and so if it meets all those criteria of an LDT, the labs simply notify the FDA within five days of when they begin testing. Or if they've already begun testing, within five days of the guidance. And I believe that's today if they were testing before [INAUDIBLE].

CDR Kim Piermatteo: Hi Tim, you're cutting out a little bit. We're having some difficulty hearing you.

Timothy Stenzel: Yeah. I am sorry, thanks for alerting me.

Eugean Jiwanmall: Yeah, thank you so much. I know Tim is having issues with that. So I do get the general answer, I do appreciate it. Kimberly, I just-- the main part for the first question that Tim was answering was that after our last submits for five-- within five days, which is today or [? Wednesday-- ?] started offering it the data that is submitted for validation to FDA, if FDA reviews it, what do they do with it? And if it is not up to par, is there going to be some sort of notification from the FDA publicly that this submitted-- because they're not going through the EUA process that this submitted data is not up to par. That's what I was looking for, then what is FDA going to do with that validation data that is submitted for them within five days?

Toby Lowe: OK, so this is Toby. I can give a little bit more on that. So generally, we-- I think your initial question-- I just want to make sure that we also clarify you were asking if EUAs-- if your understanding was correct that EUAs were not required other than for those that we're prioritizing, and that's not quite accurate. We are generally expecting tests to be authorized or cleared prior to being offered or distributed unless they fall into one of the specific policies laid out in the guidance.

So as you noted, for lab developed tests, and as Tim was talking about, if a test falls under the type of test that is laid out in the guidance-- so high-complexity lab, single site, molecular PCR or lesion swabs-- and they notify us within those five business days, then we intend not to object, which is sort of the legal language for we don't expect an EUA for those-- for those tests. And so for those notifications from the labs, if you look at the information that we're asking be submitted in-- in the notification, it actually does not include the validation information.

So we're not expecting to get the actual validation data from those labs. We're asking just for the labs to confirm that they have appropriately validated their tests. So we will not be reviewing validation data for those. We do intend to reach out to a lab if we get signals that there is a problem or a concern with a test; then we do intend to work with the laboratory to address that concern. And if it can't be addressed

adequately in a timely manner, we would expect the lab to take appropriate steps to address that, such as stopping offering the test, notifying users of corrected test reports, and whatever is necessary depending on the issue.

Eugean Jiwanmall: Thank you so much, Toby, that was very, very helpful because that was a thing that we wanted to clarify. That's terrific. Just one last piece. So I understand validation data is not going to be there, but the labs that do submit to you within the time parameter, within the five days, is FDA going to have a running list of them available publicly, that these labs have submitted-- that they're doing a test, LDTs?

Timothy Stenzel: Yeah

Eugean Jiwanmall: So--

Timothy Stenzel: Yeah, this is Tim. And we're going to need to move on to other questions here soon. Hopefully you can hear me now, I'm connected in a different way. Toby, am I coming through OK?

Toby Lowe: Yes, yep.

Timothy Stenzel: OK, all right. Yeah, so the FDA intends to look into posting the notified labs, and I can't give you a time on that. All right, let's move on to the next person with a question.

CDR Kim Piermatteo: Great. Thank you, Tim and Toby. All right, our next question is coming from Susan. Susan, I have unmuted your line. Please unmute yourself and ask your question.

Susan Sharp: Hi. Thank you, thank you guys again for these calls, again. Simple question. If a lab was using the CDC assay-- and understand that is the CDC's call to make. But if they're using that assay, is it possible to do more of a small bridging study to use an alternative viral transport medium like UTM or M4 or UVT rather than just the CDC recipe for viral transport media? Thank you.

Timothy Stenzel: You know, I would reach out to the FDA to discuss how we would recommend validating an additional transport media. You can also reach out to the CDC. I know that they're contemplating such questions, but I can't speak for them.

Susan Sharp: OK, thank you very much.

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

Min Yao: Yes, thank you so much. This is Min Yao from PureVision AI. We have access to this leftover monkeypox specimens, but they don't have IRB approval. So my question is, can we use them for the clinical study? Or if not, can we use them for analytical performance evaluation? Thank you.

Timothy Stenzel: I would check with your IRB. Usually residual de-identified samples can be used for activities such as test validation. But some local IRBs may ask for a review and a waiver of consent for that. So just check with your local IRB. The FDA does not weigh into that for this.

Min Yao: Thank you.

CDR Kim Piermatteo: Thank you, Min, thank you, Tim. All right, our next question is coming from Shyam. Shyam, I have unmuted your line. Please unmute yourself and ask your question.

Shyam Saladi: Thank you for holding these meetings. I'm with a-- I'm calling about-- my question's regarding development of alternative test methodologies like antigen, lateral flow antigen tests. FDA has put out templates for COVID for this, but no such ones for monkeypox. Could you please provide input on how the FDA would provide input on validating such a test?

Timothy Stenzel: Yeah, as I stated in my opening remarks, the FDA is working on a template for rapid antigen tests. You can-- if you have BSL3 capability you can use cultured virus to begin your work on that. You can use cloned expressed protein to begin your work there. We are going to seek-- we're all going to recommend that you contact ITAP. They're open for applications now, so if you're interested you should apply or begin the application process as the method to validate and-- and seek authorization for rapid antigen tests as we did for COVID. The ITAP program is open. And-- and then we'd also expect that the validation will be on actual patient material for rapid antigen tests rather than contrived, as we're allowing for-- for molecular tests for lesions. Thank you.

Shyam Saladi: Thank you. Just one quick follow-up. With regard to usability studies, is-- do you have a sense of when that input might be released?

Timothy Stenzel: So the workflow is different than COVID. So the usability piece around whether a home user can do this adequately-- if it's point of care, we're going to want to see a point of care site testing but usability is expected. Kris, any further updates on that?

Kristian Roth: You did break up, you broke up there just for one second. I believe it was about POC?

Timothy Stenzel: Yeah.

Kristian Roth: I don't think we have anything more than is in the template right now. Of course, you can always submit specific questions with proposals to the MPXDx email address.

Timothy Stenzel: Thanks, Kris. Yeah, we're going to get out the rapid antigen template as soon as possible. But I think—

Shyam Saladi: Thank you.

Timothy Stenzel: --on to the next question.

CDR Kim Piermatteo: Thank you, Tim. All right, our next question is coming from Deb. Deb, I have unmuted your line. Please unmute yourself and ask your question. Deb, it looks like you may have hit the wrong button. I'm going to unmute you again and allow you to talk.

Deb Wadford: Is that better?

CDR Kim Piermatteo: Yes it is.

Deb Wadford: This is Deb Wadford from the California Department of Public Health. Appreciate this call. Quickly, you're very-- your instructions are quite clear on the lesion sample type for EUAs. My question is, what about those laboratories now doing testing for mpox and orthopox that are using non-lesion specimens? What are the ramifications of this invocation of the EUA? Thank you very much.

Timothy Stenzel: So we expect the labs that have already been testing to notify us and reach out to us if-- if they're testing lesion swabs only. If they have alternate sample types they need to notify us and reach out to us about their alternative sample types.

Deb Wadford: Thank you.

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

Landon Stovall: Hi, this is Landon Stovall from Pandemic Response Lab in New York. My question refers to the summary and the template. So the summary document says to refer to Appendix A on the template regarding multiple plex-- multiplex panels, and then Appendix A lists reproducibility and repeatability but I don't necessarily see guidance for that within the template. I was wondering if there was guidance for reproducibility and repeatability, or if there is a difference for multiplex assays?

Timothy Stenzel: Kris, are you able to respond to that?

Kristian Roth: So you're talking about the monkeypox multiplex assays?

Landon Stovall: Correct.

Kristian Roth: Yeah, I'm not-- I wouldn't be able to respond to that right now, but you could certainly send that in. We can get back to you quickly.

Landon Stovall: Thank you.

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

Penny Houston: Hello, can you hear me OK?

CDR Kim Piermatteo: Yes, we can.

Penny Houston: Awesome. Yes, my name is Penny Houston, I am from Villa Diagnostics. I just have one quick question, and thank you-- before I ask, thank you for providing all this great information. It's really very useful. I'm looking at your template and you-- there is the ability to use the contrived samples, but it is a condition of authorization. And I was asked-- I would like to know if the agency has some expectation for timing for that post-market study? Or should we just work with you individually?

Timothy Stenzel: Just work with us individually, and we'll work out timing on that.

Penny Houston: OK, thank you very much.

CDR Kim Piermatteo: Thank you, Penny. I think, Tim, we have time for one more question so I'm going to unmute the line for Rainer. Rainer, I've unmuted your line. Please unmute yourself and ask your question.

Rainer Ziermann: Hi, thank you very much for taking my call. I have a brief, quick question, a practical question regarding negative specimens. What is considered the appropriate clinical negative specimens for the clinical validation? Is it a non-monkeypox lesion swab, such as a swab from a mosquito bite or a spider bite, or what is all included in that? Thank you.

Timothy Stenzel: Yeah, anything that a clinician thinks is a skin lesion swab. I mean, I would think things like-- that a lab that's doing this kind of testing would have herpes lesion swabs, or even something like syphilis that-- that can act as mimics for monkeypox would be the most prevalent in the lab. But any skin lesion negative for monkeypox. It can be positive for something else, just negative for monkeypox.

Rainer Ziermann: Great, thank you very much.

CDR Kim Piermatteo: Thank you, Tim, thank you, Rainer. That was our last question for today, so I want to thank everyone for your participation. And again, a huge thank you to our panelists Tim, Toby, and Kris. For your information, printable slides for today's presentation were posted to CDRH Learn at the link provided on this slide under the section titled Specialty Technical Topics, and the subsection Public Health Emergencies. A recording of today's webinar and transcript will be posted to CDRH Learn under that same section and subsection in a few weeks.

If you have additional questions about today's webinar and monkeypox test development and validation, please send an email to MPXDx@fda.hhs.gov. Upcoming town halls and other CDRH webinars will be announced on the CDRH's Medical Device Webinars and Stakeholder Calls page, which we provided the link on this slide as well.

And as Tim and Toby had mentioned earlier, we will be hosting another webinar next week on the topic of monkeypox again, on Wednesday, September 21, 2022 from 12:05 to 1:00 PM Eastern time. As Tim mentioned as well, the next combined monkeypox and COVID webinar will be on September 28 at the same time. Thank you all again for joining us. This concludes today's webinar, and we hope you have a wonderful day.

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