Virtual Town Hall #71
October 06, 2021

Moderator: Joseph Tartal

Joseph Tartal: Hello, and thank you for joining us today. I'm Joseph Tartal, Deputy Director in the Division of Industry and Consumer Education in CDRH's Office of Communication and Education, and I'll be moderating today's program. Welcome the virtual IVD Town Hall Number 71 for SARS-CoV-2 test developers, in which we'll discuss and answer your questions about diagnostic tests in the fight against COVID. The next IVD Town Hall will take place on Wednesday, October 20. Today's presentation and transcript will be made available at CDRH Learn under the subsection title, Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series.

Please note, the August recordings and transcripts are now available, and we're currently working towards making the September transcripts and recordings available as soon as possible. Our panelists for today's program are Toby Lowe, associate director for regulatory programs in the Office of In Vitro Diagnostics and Radiological Health or OIR, and CDRH's Office of Product Evaluation and Quality, and Dr. Kristian Roth, also from OIR. We'll begin with opening remarks from our speakers. And then we'll answer your previously emailed submitted questions about COVID test development and validation.

And then finally, we'll open the line up your live questions. To ask a live questions, please select the Raise Hand icon at the bottom of your screen when we get to that part of the program. When you're called on, please identify yourself and ask your question promptly. Also please note we're not able to discuss specific submissions that are currently under review. With that, I will hand the program over now to Toby. Welcome, Toby.

Toby Lowe: Thanks, Joe, and thanks, everyone, for joining us again this week. We do have several updates to share and then we'll get into the questions, as Joe said. So first you may have noticed that yesterday we updated one of our FAQs. It's the FAQ related to-- sorry I think this was Monday, actually, not yesterday-- but the FAQ related to how we prioritize review. That was updated to indicate that for at-home tests and home collection tests, we are prioritizing diagnostic testing there. So we are not prioritizing home tests or home collection for serology or antibody tests at this time. We will continue to evaluate the priority there for those types of tests. And corresponding to that FAQ update, we removed the serology home collection EUA template, from the website, just to avoid any confusion there.

So then this morning, we updated all of the remaining templates on our website. We added a cover sheet template for molecular diagnostic EUAs, EUA requests. And we updated all of the remaining molecular antigen and serology templates. You will see a lot of changes if you were to do a red line compare, if you've saved an old version. But these were primarily updates to bring these current, provide clarifications, add information in areas where we've had a lot of questions to help streamline the process.

There were no major policy changes in these updates. The performance recommendations primarily remained the same. But some of these hadn't been updated in several months, and we wanted to make sure that they included all of the most current information. So those can be found in the same place on the website.

The next update we have is that on September 23, so just after our last town hall, we issued an EUA revision that applied to most previously authorized molecular, antigen and serology tests for COVID-19 to add conditions of authorization regarding viral mutations. So this revision was intended to bring all of the EUAs up to where we currently are since we've started adding conditions of authorization related to viral mutations in recent months to new authorizations.

So it adds conditions related to monitoring of emerging viral mutations and their potential impact on the performance of authorized SARS-CoV-2 tests. And it also requires developers to update their test labeling regarding the impact of potential viral mutations.

So the next update is earlier this week on Monday, we authorized the Acon Laboratories Flowflex COVID-19 home test, which is an over-the-counter antigen test. It can be used for both symptomatic and asymptomatic without the need for serial testing. And we announced in the press statement that the company is expecting significant manufacturing capacity, so we expect that this authorization should double rapid at-home testing capacity in the US over the next several weeks.

And then yesterday, we issued a safety communication related to a recall that Ellume put out for the Ellume COVID-19 home test. There was a recently identified manufacturing issue that led to a potential for false positive results with certain lots of the Ellume home test. So Ellume issued a recall on Friday, and we put out the related safety communication yesterday. So all of those can be found on our website as well. And hopefully, those updates will be helpful to folks.

So now we can go into the prepared Q&As, the ones that we've received ahead of time. As usual, we will caveat this that we sometimes receive questions that are a little too detailed or case-specific, so we won't address those on the call, and we'll try to address those in writing. And if you have additional questions or don't receive an answer to your question, please feel free to reach back out to the CDRH-EUA-templates@fda.hhs.gov mailbox for an update. And as we get into the questions, I will ask Kris to take the first one.

Kristian Roth: OK, great. Thank you, Toby. So the first one is concerning the letter from September 23. That is the Amendment. This is talking about condition 2 of that letter. And in condition 2, there's a statement there that says for multi-analyte tests, you must evaluate the impact of SARS-CoV-2 viral mutations and all other target analytes. And so she's asking for more clarity around that.

And so if your test does detect more than one analyte, developers should include all targets in silico evaluation of inclusivity and cross-reactivity performance. The frequency of this analysis after you receive your EUA may differ depending on the analyte. So for instance, mutations impacting a flu target may only need to be assessed on a longer time period than SARS-CoV-2.

The question goes on, says, for example, for a COVID-flu combo test, is the expectation to A, monitor the impact of SARS-CoV-2 viral mutations on flu performance, or B, monitor the impact of flu viral mutations on flu performance. So indeed, the expectation is to monitor both of these issues-- the impact of the SARS-CoV-2 virus mutations on flu performance and the impact of flu viral limitations on the flu analyte performance as well. However, your monitoring procedures should follow a risk-based approach, which includes an evaluation of the current published literature, periodic in silico analysis, and other sources of information that you may have available to you to kind of guide the frequency depth of the analysis that you're performing you after you receive your EUA.

The focus of this amendment was certainly SARS-CoV-2. However, we are including all of the target analytes as well to kind of be make sure this is a comprehensive approach. But again, I think the focus is SARS-CoV-2, because that is certainly the need right now. With that, I'll turn it back to you Toby. Thanks.

Toby Lowe: Thanks, Kris. So our next question is regarding seeking 510(k) clearance for a multiplex flu AB and SARS rapid antigen detection assay. The question starts out asking if it's acceptable to use an EUA-authorized multiplex flu AB SARS RT-PCR as a reference for all three targets or whether the flu AB reference has to be an FDA-cleared test. And also asking if the same applies for discrepant testing. So we do expect the comparator for flu AB to be an FDA-cleared device, and that is the same both for your comparator method and for discrepant testing.

The question goes on to ask, since there's no cleared SARS-CoV-2 assay using nasal swabs as a sample type, is a single rather than a composite EUA-authorized SARS-CoV-2 RT-PCR assay acceptable as a reference for the SARS-CoV-2 target? Yes, it is acceptable to use an authorized an EUA-authorized SARS-CoV-2 RT-PCR as the reference.

And then the last part of this question is whether the reference RT-PCR that they're looking to use does not have claims for a specific specimen type, but the reference lab has validated that specimen type, is it acceptable to use the results from the lab-validated specimen as a reference. No, it would not generally be acceptable. We do expect your comparator method to be an authorized assay, either a cleared or approved assay or an EUA-authorized assay. And that it is fully authorized for the proposed specimen type. And we would expect the comparator to be used as authorized when doing the study. Kris, anything you want to add on that one?

Kristian Roth: Yeah. Thanks. There's a lot going on with this question. I think there's a lot of details and options that could be discussed in a Q-Sub. And that's likely a better source of information if you're going to go for and design a 510(k) study. I'm taking, I guess, kind of brief answers on this call. So really, use that Q-Sub process. We have a fairly streamlined approach. We'll get you back about recommendations fairly quickly. Thanks.

Toby Lowe: Thanks, Kris, that's a really good point, and brings up another topic that we should touch on briefly, since we are getting a lot more questions about transitioning from an EUA to full marketing authorization through clearance for PCR tests, molecular tests, and likely, for a De Novo for antigen and serology, at least for the first ones, and then 510(k) follow-ons. We do recommend Pre-Subs for those. And we also want to make sure that folks are aware that the decision summary for the Biofire De Novo that was authorized is posted on our website. And that includes a lot of useful information to see what we reviewed and what the differences are between what we are looking at under an EUA and what we've reviewed for full marketing authorization. So we would recommend that developers looking to make that transition take a look at that decision summary, and then reach out through a Pre-Sub with additional questions.

So moving on to our next question. This one is asking whether FDA is considering unsupervised self-collection and home collection using a throat swab. And the answer there is no, we generally do not believe that throat swabs are appropriate for self-collection. If performed incorrectly they can cause harm. And we agree with our colleagues at CDC, who recommend that throat swabs be collected by a trained health care provider.

Our next question is asking about whether it's an option to collect samples in a subject's home for a point-of-care trial. They would plan to send a trained clinician or staff member to the subject's home, and that they would plan to do a separate home use trial at a later date. So generally, that would not be considered appropriate. We think that a point-of-care clinical study really should be conducted at the point-of-care clinical site where study participants are conducting specimen testing as part of their routine clinical duties. That test performance is often impacted by the use setting, and so that should be evaluated during the clinical validation study.

The next question is about a rapid antigen device that was submitted for EUA with an intended use for symptomatic patients, but they are looking to expand to asymptomatic. And they've seen that the recent authorizations are better for asymptomatic include serial testing. So they're asking about how to proceed there.

So we would recommend that you take a look at the supplemental template for developers of molecular and antigen diagnostic COVID-19 tests for screening with serial testing, which includes guidance regarding serial testing. We do not require that asymptomatic individuals be tested serially, but that is an option for mitigation to get an authorization for screening if you don't have asymptomatic data. So you can discuss this further with your reviewer, but if you have data that meets the bar that we've recommended in that supplemental template, then proceeding with serial testing is an option as you continue to collect asymptomatic data.

Our next question is regarding an EUA for an over-the-counter antigen test with different packaging configurations of different numbers of tests, and asking whether they need to include different configurations in the usability testing. And then further asking if for over-the-counter usability and comprehension studies, would the study need to be repeated or restarted if there were changes to the Quick Reference Guide.

So this is something that is going to generally be specific to your case, and we would recommend that you come in to discuss this a little bit further, since it will depend on how the different size packs are configured and what changes are made to the Quick Reference Guide. If the configurations are simply just adding more quantity together, then it may not be necessary to incorporate that into your usability testing. But if the configuration changes the size of the reagent bottles or the packaging, then we may want to see that included in the usability testing.

And then the last question that we have here is regarding the September 23rd revision to add additional conditions of authorization related to viral mutations. Specifically, that one of the conditions asks for submission of a supplement within three months to include specific language, and asking whether a supplement is still required if the manufacturer's labeling already includes the language.

So we would ask that the sponsor notify FDA, that you believe that your labeling already addresses the requirements outlined in the condition. And then we will get back to you either saying that we agree with you or asking for any updates that we think are necessary. And with that, and we can open things up to live questions.

Joseph Tartal: OK, so thank you, Toby, and thank you, Kris. And we'll go to our live question and answer portion of the program. As was stated in the beginning, please raise your hand. Once you've raised your hand, I will click on that name, and open up allowing you to talk. Please unmute yourself and ask your question. So with that, Michael, I'm opening up the line to you.

Michael Dubrovsky: Hi, can you hear me?

Joseph Tartal: Yes.

Michael Dubrovsky: Great. I just have a question. There's some information on the FDA website about potentially providing EUAs for COVID severity testing. And I'm from a company called Sci Fox and we have an inflammation test that can be used at home or a point of care that we're developing. And we're curious about whether the FDA sees that as a big need, for example, for triaging people to get monoclonal antibody treatment or whatever it might be-- the route if they're likely to have a severe outcome. So how is that viewed, and is there any guidance on what you'd be looking for in an at home version of that test or some kind of point of need version for pharmacies, where people, if they get tested positive, can get a test and see if they need to see a doctor or get further investigation?

Toby Lowe: Thanks for that question. So we do have a few IL-6 tests that we've authorized through the EUA process. And generally, for tests of that type, we would ask that you submit a pre-EUA since we don't have templates up for those, and we think that having a more targeted discussion about what you're looking to do is going to be beneficial.

Michael Dubrovsky: OK, that makes sense. And then just a follow-up question-- is IL-6 the only target you're open to? Or for example, like CRP, which is used in Europe and China, is that a possibility or other targets? Do you have a narrow focus on IL-6?

Toby Lowe: That's what we've seen so far or what we've authorized so far, but we would encourage you to come in and discuss if you have alternatives that you think would be beneficial.

Michael Dubrovsky: OK, thank you.

Joseph Tartal: And with that, we'll go to our next question. Shannon, you're now opened up. Please unmute yourself and ask your question.

Toby Lowe: Shannon, we can't hear you yet. Maybe you are on double mute.

Joseph Tartal: Are you there, Shannon? And we'll go on to our next question. So Christie, I'm going to unmute. Please ask your question and unmute yourself.

Christie Bergerson: Hi. I think I'm unmuted. Can you hear me?

Joseph Tartal: Yes.

Christie Bergerson: So I have a question about the topic that you just brought up. So when developers do encounter these viral mutations and they do this analysis to see whether or not their tests are impacted, they then have to update the labeling. I'm assuming that the labeling would say something like this is effective even with the Delta variant or something like, that and you would expect that to be reflected in their instructions for use and maybe on their outside packaging. Is that correct?

Toby Lowe: So far, what we've done is the monitoring that we've had developers do is to see if there's a risk that their test would be negatively impacted by any known mutations. So if that comes up and we

find that the test is impacted by a particular mutation or mutations, we would work with the developer to address that issue, whether it's through modifying the test or modifying the labeling.

We have not asked for updated labeling to say proactively that a test does detect specific variants. We have instead asked for the labeling to be updated as outlined in the conditions of authorization to specify that it has not been validated in all circulating variants. And Kris, do you want to add anything to that?

Kristian Roth: Sure. Your performance in your label should be maintained. And so it should be maintained regardless if it's Delta or some other kind of variant. So that's already kind of in your label. Now if there's some reactivity change or there's some issue where you're going to get some type of result with a variant, that's something that obviously is a change to the assay performance, and we would want updated in the label. You should be detecting Delta, you should be detecting whatever the circulating strain is. Or if not, then that's where we really want to get that label updated and see if there's any further information it can provide.

Christie Bergerson: OK, so it's not permissive like I was thinking. It's more of a warning.

Kristian Roth: Correct.

Christie Bergerson: Got it. OK, thank you very much.

Joseph Tartal: Thank you for your question. I'm going to unmute Shannon again.

Shannon Clark: Hello, hello, it's Shannon Clarke. Can you hear me?

Toby Lowe: Yes, we can.

Shannon Clark: Yeah, I had called in, so that was my problem that I was trying to talk over the phone. But this is Shannon Clarke with UserWise Consulting. We specialize in home use testing. My question is about OTC clinical evaluation testing of antigen and molecular home use products.

All-comers format is really important for making sure you're getting sort of a representative slice of the population with regards to their viral loads. If we recruit people to join this study, but there's a lag between when we first get on the phone with them to recruit them and then when they actually show up to the study, is that a problem? Is there a minimum or maximum-- is there a maximum lag between their initial inquiry and when they're tested that is acceptable to the FDA?

Toby Lowe: Kris, do you want to take this one?

Kristian Roth: Sure, I'd say at the time of the moment, that individual needs to meet the enrollment criteria. And whatever that is, you're going to have your typical criteria, and that needs to be met at the time of enrollment in the study.

Shannon Clark: But we typically don't have any requirements for OTC use-- that they must have symptoms within the past seven days and so on and so forth.

Kristian Roth: I think that's somewhat of a different question. You need to have enrollment criteria that that's sufficiently defined for the intended use population you want to study. And that should be something-- you got questions, we can obviously discuss that in the context of that particular test. But I think the original question is they should be meeting the enrollment criteria at the time of enrollment.

Shannon Clark: I see. I'm just wondering what the enrollment criteria should be with regards to when they first inquired to participate and then when they actually participate. So it sounds like there should be an enrollment criteria surrounding that? So I guess I'll send an email.

Kristian Roth: Yeah. Sure, I guess a typical enrollment criteria is asymptomatic or no known infection within the last three months or something of that nature. And if there's a month-long lag between you first identify the folks and when they're enrolled in the study, then you need to reconfirm those kind of time-dependent enrollment criteria.

Shannon Clark: All right, thank you.

Joseph Tartal: Thank you. We'll move on to our next question. David, I'm going to unmute your line. Please unmute yourself and ask your question.

David Brooks: Hi, this is David Brooks, Biocrucible in Cambridge. I wonder if you have any guidance or expectation around a two-target approach for molecular testing, and furthermore, is any difference in that approach between EUA and 501(k).

Toby Lowe: So I'm not sure that I'm exactly following your question. We do have recommendations in the EUA template for what we're looking for validation, and we do recommend multiple targets as one of the mitigations against an impact of viral mutations. Is there a specific recommendation or specific items that you're looking for?

David Brooks: I'm looking for what's the absolute requirement here.

Toby Lowe: So we provide recommendations. We don't have absolute requirements. But we do recommend multiple targets.

David Brooks: Understood, thank you.

Toby Lowe: Kris, did you want to add anything to that?

Kristian Roth: No, not really. This honestly is a recommendation. We believe that the multitask test is more robust, but if you've got a single target, you think it's well-conserved, you validated it, and you have a plan to monitor for variants, it's certainly something that we have authorized in the past. There are single tests out there that are available. So as to we mentioned, it's not a requirement. This is kind of a scientific issue.

It's good to have a backup target. You're asking about 510(k) as well, and I think it applies the same way to 510(k). There is certainly no requirement about how many targets you have per analyte. And that's been true for many tests, not just for respiratory tests as well.

David Brooks: Thank you.

Joseph Tartal: Thank you. We'll move to our next question. I'm going to allow you to talk, Ivory. Please unmute yourself and ask your question.

Ivory Chang: Yes, this is Ivory Chang. I'm asking questions regarding the swab. So we would like to know from the FAQ recommendation, generally, they require a full-size tip for the anterior specimen collection. However, we would like to know, will we be able to use a pediatric swab, which is a mini tip for the anterior type specimen collection. Does FDA have any concerns-- and this is for a home OTC COVID molecular test?

Toby Lowe: Thanks for that. So we would ask that you submit a pre-EUA, since this is a very specific question related to your test. But generally, if you're using sort of an alternate swab type, we would expect you to validate it and use it in your clinical study and your usability, and demonstrate appropriate validation. But I think that is something that is probably worth sending in a pre-EUA, since that's very specific.

Ivory Chang: OK, that's great. Yeah, we will do that. Thanks.

Joseph Tartal: OK, next question. Ron, please ask your question. I'm unmuting you now.

Ron, please unmute yourself to ask your question.

Ron Domingo: Can you hear me now?

Joseph Tartal: Yes.

Ron Domingo: OK, great. So as a way of background, in April of 2020, we were told for a molecular assay to be considered high sensitivity, it would have to be at least as good as the CDC test. And that's 10,000 NDU per mil. So we reran the samples against the CDC assay and we received authorization. Now in October 2021, we were told that the CDC assay was not sensitive enough as a molecular comparator and we were denied authorization. So my question is what is the FDA's sensitivity in NDU per mil that is considered as a high sensitivity molecular assay for use as a competitor? Thank you.

Toby Lowe: So I can start this off, and then Kris, if you want to add anything. We don't have a specific cut-off that we've provided. I think Tim, Dr. Stenzel, has talked about this on the call previously. As you've seen, things change throughout the pandemic. Benefit-risk calculations changed based on where we are and how many tests are available. So that is something that we would recommend that you send in a question to the mailbox with specific tests that you're considering as a comparator, and we would be able to get back to you on whether we consider them to be appropriate competitors at that time. Kris, do you want to add anything there?

Kristian Roth: Yeah, there must be a missing piece of information here. CDC assay-- singlepex assay is a comparative method that has been used by many different companies. That's a few different applications, so I'm not sure what the conflict here really is.

Toby Lowe: Yeah, so there may have been some miscommunication. If you want to send in a question, you can ask that Kris or I take a look at it.

Kristian Roth: I'm glad to. If you want to mention my name, I'm glad to take a look as well.

Ron Domingo: All right, thank you.

Joseph Tartal: Thank you. Next up again is Shannon. I'm going to open up your mic. Please unmute and ask your question.

Shannon Clark: Hello, hello, Shannon Clark, UserWise Consulting. My next question is quite simple. Can an OTC IVD product for over-the-counter use be refrigerated upon storage and after purchase by the end user? Or is there an expectation that it must be shelf stable and shouldn't require refrigeration?

Toby Lowe: Sorry, you're asking if an over-the-counter test can require refrigeration?

Shannon Clark: Exactly.

Toby Lowe: That's probably something that we will need to consider, but I think that's not something that we would typically think is appropriate for over the counter. So if there's some additional reason why that might be needed, we would want to have some further discussions with you on that. But generally, we would expect over-the-counter to be shelf stable.

Shannon Clark: Thank you. That's what I anticipated. Do you happen to know of any OTC products that must be refrigerated?

Toby Lowe: Not off the top of my head. Kris, do you?

Kristian Roth: No, I don't. I mean, that would be a little bit unusual. It would be unusual, yeah.

Shannon Clark: Excellent. Thank you so much.

Joseph Tartal: Thank you. And next up, Ariane, I'm going to unmute your mic. Please ask your question.

Ariane Erickson: Awesome, good morning. I just have a quick question on choosing an appropriate comparator test. So we have an antigen-based lateral flow test, and we use nasal swabs for sample collection. Do you anticipate any issues if we use an EUA-approved PCR test that uses a different sample collection like saliva?

Toby Lowe: So we do have recommendations in the templates regarding appropriate comparators. Typically, we would consider nasopharyngeal to be the best comparator. And I believe we also would accept nasal swabs as a comparator. Saliva, we typically don't consider to be the best comparator, so we would encourage you to look at that nasal or nasopharyngeal. Kris, do you want to add anything there?

Kristian Roth: No, that's right.

Ariane Erickson: Perfect. Thank you.

Joseph Tartal: Next up, Tianyang Liu, I'm unmuting you now. Please unmute and ask your question.

Tianyang Liu: Thank you. So my question is for the OTC over-the-counter test kit. If the enrollment strategy is for all-comers, is it necessary to exclude the subject with non-COVID-19 status to control the bias.

Toby Lowe: Sorry, to exclude with what?

Tianyang Liu: Exclude patients who knows their COVID status, who already know the results.

Toby Lowe: Aha. Yes, generally, we would not want those types of patients to be included.

Tianyang Liu: So just do not include those who know their condition to the clinical trial, right?

Toby Lowe: Right, right. Kris, do you want to add anything on that one?

Kristian Roth: And especially if it's a visually read test. That's really an opportunity for bias to kind of creep into the interpretation. If they know that they're positive, and they don't see a line. Or vice versa, that kind of biases that evaluation of a test result.

Tianyang Liu: OK, so in this case, if we already included some, what should we do? Should we exclude those in the data analysis when preparing the report?

Kristian Roth: I wouldn't exclude it. I would just note that these are the individuals that knew their status beforehand, and you can analyze the data with and without that. And just make sure that that's obvious in the line data when you submit it to us.

Tianyang Liu: OK, so if the FDA asked us to add new enrollees, add new subjects as a supplement, if we want to apply this exclusion criteria, should we exclude the individuals who have been tested within the last three days? The three days is enough or not, if we need to exclude those ones?

Kristian Roth: That's a good question, and I think that's probably worth an email for us to kind discuss with the antigen team specifically. I know there's been different proposals and different frames. So I think you could send that and you can ask it sent to me, and then I can get an answer for you from the antigen team.

Tianyang Liu: Thank you. So you mean copy who?

Kristian Roth: KristianRoth@fda.hhs.gov.

Tianyang Liu: OK, Kristian Roth. And actually, we have send this to the template before, and the template said that we should send the pre-EUA.

Kristian Roth: Sure. Yeah, you can do that as well. If it's just a single question, sometimes we can handle that just with an email. And then maybe more.

Tianyang Liu: Yeah, very simple question-- should we do three days or 14 days? Is longer the better-- is it the longer days, the better?

Toby Lowe: I think if you send that in-- send it into the mailbox and ask that it be sent to Kris and I, we can make sure that that's addressed and that the antigen team is able to weigh in on that.

Tianyang Liu: OK, thank you.

Joseph Tartal: OK, thanks. And our next question. Dana, I'm unmuting you now, so please unmute and ask your question.

Dana Hummel: Hi, can you hear me?

Joseph Tartal: Yes.

Dana Hummel: Great. My question is regarding the performance requirements for an OTC home use antigen test and clarification of the serial screening requirement. So if the clinical evaluation study includes both symptomatic and asymptomatic positive patients, and the performance is greater than 90% for sensitivity, then serial testing indication is not required, correct?

Toby Lowe: I would have to look at the template to get me to check those numbers, but that sounds right to me. Serial testing is an added option if the data is not there to support single use testing.

Dana Hummel: OK, so the second part of the question would be if we are not able to collect at least 10 asymptomatic positive patients during the study, however, our PPA is still greater than 90% for the symptomatic patients, can we still proceed with an indication of using only one test and not be required to do serial testing?

Toby Lowe: So this is something that we would work with you on during the review. So I think you can submit what you have and request the indication that you would prefer, and once we're able to take a look at your data, we'll be able to work with you on what indication is supported, and whether there's a need for any post-authorization data collection. Or if we can support an authorization with some supplemental collection post-authorization or whether we would ask that you collect some additional data before we're able to authorize it. So that's something that would be specific to your test and the data, so we would ask you to submit what you have. And we'll address that during the review.

Dana Hummel: OK. And is there a specific sensitivity requirement for the asymptomatic population?

Toby Lowe: Yes, it is in the template. I don't recall it off the top of my head. I think 90%, but I would need to double check that. But it is in the template.

Dana Hummel: OK, thank you very much.

Joseph Tartal: OK, Michael, you're up next. I'm unmuting your phone now. Please unmute yourself and ask your question.

Michael Patz: Yes, hi, thank you. I would just curious as to what FDA's position is at this time-- are they recommending manufacturers file 510(k)s or are EUAs still the priority?

Toby Lowe: So we've talked previously on here about the priorities that we are focusing on. And that is specifically, we are focusing quite a bit on tests that increase accessibility such as point of care, home

collection, at-home testing, and increase test capacity. So high throughput, widely distributed. And so we do think for those areas where it's beneficial to public health to increase availability that EUA is still likely to be the fastest pathway, but we certainly are welcoming 510(k) submissions as well. And it depends on what data collection you already have, and what is supported.

Michael Patz: If I could just ask a follow-on question then. So if a manufacturer submitted a 510(k), where does that fall in the review process then as a priority?

Toby Lowe: Yeah, so that's going to depend, again, on what the submission is for with the indications. And we would prioritize as submissions come in. Kris, if you add anything to that.

Kristian Roth: No, I think generally, at some point, going to want to move to 510(k)s. And so if you submit a 510(k) and it's complete and has all the data, we're going to try to address it within the time frames that are set up currently.

Michael Patz: OK, great, thank you very much.

Joseph Tartal: Thank you. And up next is Shannon. Shannon, I'm opening up your mic. Unmute and ask your question.

Shannon Clark: Shannon Clark, UserWise Consulting. Thanks so much for taking all of my questions. So at our lab, we can configure all kinds of simulated use environments-- operating room, home use environment, in point-of-care clinical contexts. I know earlier, you noted that it would be inappropriate to run a POC clinical study in the homes of users. Would it be inappropriate to run a POC clinical study in a simulation lab that simulates a POC context?

Toby Lowe: That may be something that we need to discuss in a pre-EUA way with some additional detail. We do want to see point-of-care tests studied in a true point-of-care environment. So that it would depend a little bit on whether if you're simulating just the setup, that's different than simulating the workflow of the settings. So that's something that we would suggest you come in to talk to us about.

Shannon Clark: I'm just trying to determine what environmental factors you might be concerned with, because on one hand, I want to control the experiment, you want to make sure that these individuals are not trained. But most likely, if we do run it in a point-of-care setting, they'll probably receive assistance, and there's a lot less control over the test subjects, that is, the health care providers. Can you think of a specific concern? Is that an example of an environmental factor that you'd be concerned about?

Toby Lowe: Yeah, I know one of the specific areas that we want to see is that the operators in a point-of-care setting are integrating this testing into their normal daily functions. So that's one of the aspects there. And then Kris, I don't know if you want to provide anything additional on this?

Kristian Roth: Sure, maybe I'm going to go out on a limb here a little bit and take it in slightly different direction. Validation studies should be done in the setting that they're going to be used in. And so in a POC environment, you've got the actual POC users. There's nothing needed to simulate there. You've got health providers that can take the comparative method sample. So logistically, there's not a lot of showstoppers.

Now if you thought about home validation of a home use test, then you start having some logistical challenges-- who's going to take comparative method is one. And how do you keep track of what user is testing the sample when, and their shipping conditions. So I think that's why we shifted to the simulated home use for the EUA-- was to streamline that validation process, because there were these kind of showstopper issues for validation of the home use tests.

And frankly, I think even in the 510(k) world, we're still discussing appropriate study designs for validation for home and how to kind of overcome some of those challenges. So I think that was driving it more than anything else as far as recommendations for that simulated home use foundation.

Shannon Clark: But what confuses me is why would an OTC simulated use human factors and clinical evaluation study-- why would those be sufficient for getting that POC designation automatically if you have this concern? That is, if we run OTC testing, and we automatically get that POC. So why would that be true if you're so concerned about the environment for POC?

Kristian Roth: Sure, and that's a fair point. But really, we're kind of bound by the regulatory system we're working in right now. So I think currently, if you get that OTC designation, you're kind of automatically eligible for CLIA-waived type of designation. That kind of framework is being used in the EUA as well. So it's a fair point, but that's just kind of the regulatory landscape that we're operating in right now.

Joseph Tartal: Great. Thank you so much. We're going to take one more question and I'm going to go to Rahm. So I'm going to open up your mic, Rahm. Please unmute and ask your question. Rahm, are you there?

OK, we'll go to one more question. Ivory, I'm going to open up your mic. Please ask your question.

Ivory Chang: Yes, so this is a question going back to today's earlier FDA comments. You recommend us to use a EUA authorized specimen type from a comparator. So I want to know, when we develop our test, if the comparator we selected, they are using the mid-turbinate specimen type, but we would like to go to the anterior specimen type, will we be able to do this in a clinical study? Or we have to use exactly whatever the comparator authorized specimen type? I just want to get more clarification.

Toby Lowe: So we're recommending that the comparator test be used as authorized. That does not mean that you need to run your candidate test in that way. I may have misunderstood your question.

Ivory Chang: Yeah, it has got EUA-authorized, but they are using different type of specimen type in their intended use. And for us, we would like to use a different type of specimen, as we are more appropriate to use at-home tests. But they are the highly sensitive PCR tests, which use the nasopharyngeal swab.

Toby Lowe: Yeah, so we do typically recommend nasopharyngeal as the comparator method. And especially for 510(k)s, that's likely what we will be expecting. And so as we've mentioned earlier, we do expect the comparator method to be performed as authorized. So it would not be appropriate to use a nasal swab for the comparator method, especially if the test is not authorized for that.

Ivory Chang: OK, wonderful. Thank you. That's clear. Thanks.

Toby Lowe: Great.

Joseph Tartal: OK, and with that, that is the last question of today. So thank you, everyone, we greatly appreciate your participation. Today's presentations and transcript will be made available at CDRH Learn. Please visit CDRH Learn at www.fda.gov/training/cdrhlearn. You will find the recordings and transcripts in the subsection titled Coronavirus COVID-19 Test Development and Validation Virtual Town Hall Series. Again, as previously noted, the recordings and transcripts from August are now available, and we're working towards making the September transcripts and recordings available. For additional questions about today's presentation and topics, please send an email to CDRH-EUA-templates@fda.hhs.gov.

As we continue to hold these virtual town halls, we appreciate your feedback about the program series, so please complete a brief survey which you may find at www.fda.gov/cdrhwebinar. Last, as a reminder, please join us for the next webinar town hall scheduled for October 20.

This concludes today's town hall. Thank you.

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