

## **Virtual Town Hall 8-4-21**

**Moderator: Anike Freeman**

**August 4, 2021**

**12:15 PM ET**

**Anike Freeman:** Hello. I'm Anike Freeman of CDRH's Office of Communication and Education. Welcome to the FDA's 65th in a series of virtual town hall meetings to help answer technical questions about the development and validation of tests for SARS-CoV-2 during the public health emergency. Today, Toby Lowe, Associate Director of the Office of In Vitro Diagnostics and Radiological Health, and Dr. Kristian Roth, both from CDRH, will provide a brief update. Following opening remarks, we will open the line for your questions related to development and validation of tests for SARS-CoV-2. Please remember that, during this town hall, we are not able to respond to questions about specific submissions that might be under review. Now, I give you Toby.

**Toby Lowe:** Thank you. Thanks, everyone, for joining us again this week. I don't have much in the way of updates today. But I did want to point out, I think Tim mentioned last week, that we would be adding some information to the website on the EUA tables to clarify that you can expand each row for each EUA listing. And that's where you can find things like the granting letters and additional brand names.

So that question, especially brand names, has come up quite a bit. So we wanted to make sure that was a little bit more clear on the website. And that feature or that addition to the text there went up late last week. I also want to reiterate one of the points that we made last week. We've got a lot of questions about the CDC announcement about withdrawing their EUA for their single analyte test. I just want to reiterate that that announcement from CDC and that decision by CDC does not impact any other tests. And it also does not impact FDA's review priorities.

So we can move into the questions that we got. And the first couple are actually related to that same CDC announcement. So the first one is asking if we can clarify why CDC withdrew its EUA. And that is a CDC decision, so you would have to check in with the CDC to get their reasons behind their decision making. But as I said, it does not signal any policy changes for FDA.

And then they go on to ask whether the withdrawal signals any change in prioritization policies and specifically asking whether FDA intends to prioritize multiplexed testing. And as I said, the announcement does not impact the EUA pathway for any other tests. It does not impact FDA's priorities. We've mentioned, on previous calls here, that multi-analyte tests that have sufficient manufacturing and testing capacity are included in our priorities and will continue to be prioritized. And that is not changing.

The next question that we've got has two questions, both of which were actually asked on the town hall last week in the live questions. So we can go through those again quickly. The first one is, again, about the CDC announcement asking whether the CDC test will remain an appropriate comparator for future EUA submissions provided that the study was completed prior to the CDC withdrawing their EUA.

As stated on the town hall last week, the CDC single-analyte test is still authorized. And FDA has not expressed any concern with the test. So the only implication of CDC withdrawing their EUA is that it will no longer be available after CDC stops supporting it.

And the second question from this person is with respect to the Delta variant in the US and the limited publicly available data suggesting that the viral load observed in patients is significantly higher than with the original SARS-CoV-2 virus. Will FDA be modifying the requirement for antigen tests to have 10% to 20% low positives with CT values over 30? This question, again, was also asked and answered on last week's town hall. And as we stated then, at this point, we have not modified the requirements. We do want all studies to be inclusive of a range of viral loads to be sure that the test can detect individuals within the time period for which the developer is seeking authorization. And we continue to monitor data on the Delta variant to determine if the normal distribution of results should be shifted.

The next question that we received is similar to previous questions that have been asked regarding whether the US is prioritizing multi-analyte tests and specifically asking whether we would permit a company that had a previous EUA for a respiratory panel deprioritized to resubmit the same EUA. And so to reiterate what we've previously said, multi-analyte tests that have sufficient manufacturing and testing capacity are included in our priorities and will continue to be prioritized. While we can't discuss specific submissions on this call as we've mentioned, we can generally share that if an EUA request was deprioritized previously, it was likely because the test either had low manufacturing or testing capacity or that the submission was deficient in some way. If such an EUA request was resubmitted and addressed any

outstanding issues, then it would be considered and prioritized as appropriate based on the information in the EUA request.

The next question that we have is about a rapid antigen test currently undergoing a clinical trial. They've collected more than 30 positive samples for symptomatic patients with a good distribution of CT values. But they are having some difficulties with collecting positives among symptomatic patient populations. They have a quote from the July 2020 template about enrolling at least 20 positive asymptomatic individuals and that it may be acceptable to present results from 10 with the remainder being provided post-authorization.

So they're asking whether they can submit just 10 positives from asymptomatics in their initial EUA request. Yes. If you have 30 symptomatic positives and 10 asymptomatic positives, along with a sufficient number of negative specimens, you can include that data in your EUA request with the expectation that enrollment would continue to collect the remainder of asymptomatic positives.

And just to note that asymptomatic individuals generally should be free of any symptoms of SARS-CoV-2 infection for at least two weeks prior to enrollment and testing. And as part of your clinical study protocol and data, you should document how you screened and confirmed that all enrolled individuals were asymptomatic and supportive of your proposed intended use.

The next question we have is regarding a pooling study post marketing of the product with an extended intended use claim for pooling. They want to clarify if this is related to a question that came up last week about claiming pooling for n of 3, where we had discussed on the call last week that the Supplemental EUA template does not ask for additional validation for n equals 3. And they're asking whether-- they're claiming pooling meets the agency's definition of serial testing. And if they don't add the serial claim, then does the post-market clinical study apply? So to clarify, pooling and serial testing are different indications. Pooling is combining multiple samples to test together, and serial testing is when you test the same individual multiple times over a period of days, such as every two days, every three days, or weekly.

The supplemental EUA template adds serial testing to the indication as a risk mitigation given that the template provides a pathway to add asymptomatic testing without prior validation data in that population. Under that approach, since asymptomatic data would not be validated prior to authorization, we would expect asymptomatic testing to be validated post-authorization. And

with the approach provided in that template, the serial testing is required as part of that indication to add cooling without the additional validation pre-authorization.

And the last question that we have today is about a point-of-care high throughput molecular diagnostic test, asking about the preparation of the clinical study to prospectively collect anterior nasal swab samples and asking whether it is acceptable for the company's team to help with the initial setup of their clinical testing sites, such as helping to prepare the clinical testing location and materials and answer any questions that the untrained operators may have before they begin the clinical study. So for that the, answer is generally no. For point of care, the users should not be trained. So helping with that set up would sort of negate the fact that you're studying the device with untrained users.

For high-complexity tests intended for use with trained users in a high-complexity laboratory, then it would be appropriate to provide training to study personnel, noting that any training that you provide to study personnel should also be available to your customers to ensure that the level of performance observed in your clinical study is reflective of performance in the real-world lab setting. Kris, do you have anything to add on that one or any of the responses?

**Kristian Roth:** No, I don't think. Thanks.

**Toby Lowe:** Great. Then I think that wraps up our prepared questions, and we can open up the line for live questions.

**Anike Freeman:** OK, great. Just want to remind everyone, if you do want to ask a question, please use the Raise Hand button at the bottom of your screen. Our first question is going to be from Jason Cook.

**Jason Cook:** Can you hear me?

**Toby Lowe:** Yes.

**Jason Cook:** So my question is, is the FDA still granting EUA for interleukin-6 tests for the management of COVID-19 Patients?

**Toby Lowe:** We have authorized a few IL-6 tests, and we will consider those as they come in if that's something that you're interested in pursuing. And we're generally recommending that you start with a pre-EUA to discuss your approach with the team.

**Jason Cook:** OK. Thank you.

**Toby Lowe:** Sure.

**Anike Freeman:** Our next question will be coming from John Hou.

**John Hou:** Hello. Can you hear me? Hello?

**Toby Lowe:** Yes.

**John Hou:** Hi. I'm John from [? MyoCell ?] Scientific. So our company make molecular antibodies. We're very interested in this rapid antigen test. So we actually made the antibody against a [INAUDIBLE]. And then we also have a new technology which can recognize point mutation. I figure that Delta is kind of coming quick. Do you see the need that if we could work on a maybe rapid antigen test specifically for Delta strain, or maybe other strains, do you see that need would be highly needed or not?

**Toby Lowe:** So just to make sure that I'm understanding your question fully, you're asking about developing an antigen test that only--

**John Hou:** Specifically for different--

**Toby Lowe:** Specifically detects Delta?

**John Hou:** Yeah, for different strains. So we can definitely make for a wild type, but do you see it-- I don't see anything on the market, so I'm just curious if that can be useful, if that point to the EUA too.

**Toby Lowe:** So I can start on this one and then see if Kris wants to jump in. Generally, with the virus mutating, we want to make sure that any strain is detected. So detecting whether someone is infected or not is the primary goal. And then typically, sequencing is the most effective to

determine what strain if that needs to be determined. Since if you created your test to detect specific mutations and then the virus continued to mutate, there would be additional ones that may not be caught by your test. Kris, do you want to add anything there?

**Kristian Roth:** Sure. So evaluating test performance with respect to variants with molecular tests is pretty straightforward. We've got pretty good in silico tools and methods for wet testing-- antigen tests are a little bit more nuanced.

And so I think if you have a technology that is perhaps more robust to changes in the potential epitopes on the virus and you think you've got a technology to ensure the test performance is maintained in the face of emerging variants, and that's something we absolutely would like to engage on, claiming specifically for detection, specific detection of Delta or other variants is a slightly different claim. And that would have to be validated in that particular context. So I think those are maybe the two different routes you could consider.

**John Hou:** OK. Thank you. Thank you.

**Anike Freeman:** Our next question is from Tianyang Liu

**Tianyang Liu:** Hi. Could you hear me?

**Toby Lowe:** Yes.

**Tianyang Liu:** OK, thank you. So my question is that our company has submitted the EUA for our antigen home tester kit months ago. But we just took our feedback from FDA that said it gets started and at a very early stage. Although FDA claimed the OTC home used test kit is a priority, but it seems not going that fast.

We are eager to get it approved, since we all see the Delta virus is currently spreading fast and more and more people are being infected. OTC tester kit can play a greater role against the Delta virus, because they can easily and rapidly detect the virus. Could you please let me know how much this priority bill for OTC study will speed up in the process?

And how long we are supposed to wait? Is there any kind of rough estimation for those type of EUA approval? And what kind of resources does the FDA put on the priority to speed up the OTC product? Thank you.

**Toby Lowe:** Sure. So obviously, we can't speak to specific tests. And I don't know off-hand the specific situation with yours. If you do have concerns about your file, you can send an email to the Templates mailbox and ask that it be sent to me, and I can take a look at it. But generally, OTC and home use tests are a priority. We do have a large number of submissions in the house, and we are prioritizing those reviews as much as possible and moving through them as quickly as possible.

In addition to prioritizing the home use tests, we also do look at the content of the submission. So it does make a difference if the submission is complete and followed the recommendations in the template and looks promising at first glance, if you will. And those aspects are all factored in when we have to prioritize reviews with so many submissions in-house.

**Tianyang Liu:** Oh. I see, I see. Thank you, Megan. And is your average-- I mean, average days or months that you already OTC EUA has been approved? I know that right now, we have five OTC products approved by the FDA right now.

**Toby Lowe:** So sorry, I'm not sure I caught that question.

**Tianyang Liu:** I mean, is there an average months or days that--

**Toby Lowe:** Oh. No, I can't necessarily specify a specific timeline or an average. It really does depend on the submission, the quality of the submission. And if you follow the recommendations in the template, that definitely helps to speed things up.

**Tianyang Liu:** OK. OK, thank you very much sir-- thank you very much, madam. And in this case, you said that we can send it to you. Is there an email address that we could refer to?

**Toby Lowe:** So if you send an email to the CDRH EUA Templates mailbox, it should be showing on the screen, and you can ask that it be sent to Toby to take a look and get back to you.

**Tianyang Liu:** OK. Thank you very much.

**Toby Lowe:** No problem.

**Anike Freeman:** OK. Our next question is from Michael D'Armiento.

**Michael D'Armiento:** Hi. Just clarification again on the pooling and the serial testing, if we submit with the intention to do asymptomatic serial testing and the 3 or under for pooling, no additional validation needs to be done or post-- is it automatic approval if we write in for it, or no?

**Toby Lowe:** So that is referring to the-- I think I may have some supplemental template on-- when I was responding to that question, I meant the amendment that was the Serial and Pooling Amendment that was issued recently for certain molecular diagnostic tests. So your test would be to meet the criteria that's laid out in that amendment and then follow basically the directions that are laid out in that letter of authorization for what to send in to request the additional indications from that amendment.

And if you are requesting pooling of  $n$  equals 3 and you follow everything else that is laid out in the amendment, then for  $n$  equals 3, we have not asked for additional validation.

**Michael D'Armiento:** OK. I just want to confirm that. Some of the states are giving issue with saliva testing now. And they're saying, OK, well, it needs to be approved for EUA sample. Are they're going to be a similar Amendment. For saliva testing as well or is this pretty protocol?

**Toby Lowe:** So the amendment that was issued is limited to anterior nasal swab specimens. We have seen a lot more variability with saliva as a specimen type, so we generally do want to see the validation data for that specimen.

**Michael D'Armiento:** OK. OK. Thank you so much.

**Toby Lowe:** Sure.

**Anike Freeman:** Our next question is from Junghee Kim.

**Junghee Kim:** Hello?

**Toby Lowe:** Hi.



**Junghee Kim:** Hi, [INAUDIBLE]. Thank you for taking my call. And I know Toby mentioned that the multi-analyte kits were prioritized. Is that correct?

**Toby Lowe:** Multi-analyte kits are a priority. That's correct.

**Junghee Kim:** OK. So what's your opinion on the multi-analytes on COVID-19, flu A B and RSV at the same time?

**Toby Lowe:** So we would consider that to be about multi-analyte respiratory panel. Yes. It would be prioritized. I'm not sure I'm following what the question is.

**Junghee Kim:** Oh, like necessity of the multiplex products of COVID-19 flu A B and RSV? Like, your opinion on the necessity of the multiplex of the three combos.

**Toby Lowe:** Oh. We definitely think that the multi-analyte the tests are beneficial. Chris, do you want to weigh in at all further on that?

**Kristian Roth:** I think you mentioned necessity, and that's not typically something we would comment on. If you do have a test that includes those very common upper respiratory infectious agents, that's something that we are going to review. Typically, that is flu A B, RSV, just looking at historic prevalences. So yes, that's something that's open. And we have a couple of those already authorized, and we continue to review those intended uses.

**Junghee Kim:** OK. Thank you.

**Anike Freeman:** Before we go to our next question, just want to remind everyone, try to limit yourself to one question as much as possible. Thanks. Our next speaker is going to be Wenli Zhao.

**Toby Lowe:** Wenli, I think you need to come off mute.  
Hello? [AUDIO FEEDBACK]

We can hear you, but there's a very bad echo when you speak.  
Hello? [AUDIO FEEDBACK]

Anike, maybe we can go to the next caller and then try again with Wengli if she's able to get a better connection.

**Anike Freeman:** Yes, that's fine. Our next question will be from Sam Ali.

**Sam Ali:** Hello. Thank you for taking my question. So we will be submitting a EUA for point-of-care rapid antigen test. And I just want to confirm and clarify that if we want to claim also the serial testing claim, we need to complete the usability study, correct? Submit it at the same time with the EUA for POC to get both?

**Toby Lowe:** So for serial testing, do you mean for point-of-care or for home use?

**Sam Ali:** Actually, maybe you can tell me what are the requirements for both. Because my understanding is that we need a usability study of 30 patients if we want to do the serial testing for POC and 100 for non-lab testing, so home testing. Is that correct?

**Toby Lowe:** So the usability study recommendations don't change for whether it's single-use testing or serial testing. The usability study requirements are-- or recommendations, rather-- are to make sure that the test can be used generally by the intended use population. The usability studies are done generally for home use for point-of-care.

I'm trying to refresh my memory of what we have in the template for that. We definitely want to see that the test is suitable for use in a CLIA waved setting so that it's appropriate for use with untrained users. But the requirements for that do not change between single-sample testing or serial testing.

**Sam Ali:** Right, right. So actually, the main question that I wanted to know is that if we submit the EUA package for POC and at the same time submit the data for the usability study, if everything checks, we would get both EUA for POC and a conditional serial testing until we get the asymptomatic to get the EUA?

**Toby Lowe:** So again, the usability is not what would get you the serial testing. You would want to take a look at the supplemental EUA template for what we're recommending to get the serial testing indication. But yes, if you have validation in symptomatic individuals and you take a look at the recommendations in the supplemental template, then you could use that to get serial testing

for asymptomatic individuals prior to having validation for asymptomatic-- again, separate from usability.

**Sam Ali:** Yes, correct. Yes, I understand that. Thank you. Thank you very much.

**Toby Lowe:** Great, thank you.

**Anike Freeman:** All right, let's try to go back to Wenli one more time.

**Wenli Zhou:** Hello? Is this better now?

**Toby Lowe:** Yes, a little bit better. Thank you.

**Wenli Zhou:** Thank you very much. So I have a question. I just want to get clarify for the CDC EUA test. So what I heard is CDC EUA will be taken off in the end of the year. But is the assay as a comparator still be valid, right? Say if we still have the reagent last into next year, we can still use it for the comparator assay [INAUDIBLE]?

**Toby Lowe:** I believe that what we've said is actually if it's completed while the EUA is still in effect, because we--

OK.

--so you would want to have that study done while the--

By the end of the year.

--EUA is still authorized.

**Wenli Zhou:** OK. Yeah, so this is actually while we are kind of preparing to switch to using different assay and in your table, like the reference panel, the comparative data panel. So anything higher, more sensitive than CDC so we can choose from there. Because we never figure out, what is the color of, like, higher [INAUDIBLE] sensitive assay?

So what we are using currently is a CDC as a comparator. And then if the CDC is taken off, then what we can choose is we don't want to risk to select some assay less sensitive than CDC from your reference panel. So we are trying to choose the assays that is more sensitive than CDC one. Is that correct way to think or to do?

**Toby Lowe:** Yes. We definitely recommend selecting a higher sensitivity test as a comparator. If you're looking for something with to replace CDC as your comparator, then if you look for something that has similar performance to the CDC assay, that would be a good approach.

**Wenli Zhou:**OK, great. Thank you very much.

**Toby Lowe:** Thank you.

**Anike Freeman:** OK, our last question is from Penny Houston.

**Penny Houston:** Hello there. Thank you for taking my question. I hate to ask again for clarification on the n of 3 pooling. I wanted to see-- I do have both of those documents open. And so the pooling guidance that was laid out of April 2021 this year is very clear that no validation is required pre-EUA submission for n of 3. However, I just want to be very clear that for the post-follow-up study, clinical validation is going to be required.

**Toby Lowe:** I do not-- and I'm scrolling through that amendment right now. I do not believe that there is a post-authorization data requirement for n of three.

**Penny Houston:** OK. Even if you don't-- if your original-- because it says if your original EUA does not have the asymptomatic claim, that it is recommended to do a clinical validation. So that's why I'm asking--

**Toby Lowe:** Right, so that is for the asymptomatic claim. We would want to see a symptomatic validation that is separate from pooling. So if you don't previously have-- because this amendment is only for previously authorized tests, if the previously authorized test was not already authorized for screening, we do want to see post-authorization asymptomatic validation.

**Penny Houston:** Thank you very much.

**Toby Lowe:** Yeah. For pooling, we do want to see-- we want the pooling validation to be submitted upfront. We just may not review it before-- you'll get authorized right away. We may do post-authorization audits, but those are for the n of 5 and n of 10. For n of 3, we do not have a data requirement.

**Penny Houston:** Thank you so much for that clarification.

**Toby Lowe:** Sure, absolutely.

**Anika Freeman:** Thank you. This concludes the question and answer period. This is Anika Freeman. We appreciate your participation and thoughtful questions during today's town hall. And today's presentation and transcript will be available on the CDRH Learn web page at [www.fda.gov/training/cdrhlearn](http://www.fda.gov/training/cdrhlearn) by Wednesday, August 11. If you have additional questions about today's presentation, please email [CDRH-EUA-Templates@fda.hhs.gov](mailto:CDRH-EUA-Templates@fda.hhs.gov).

As we continue to hold these virtual Town Halls, we would appreciate your feedback. Following the conclusion of this virtual Town Hall. Please complete a short 13 question survey about your FDA CDRH virtual Town Hall Experience. The survey can be found now on the [www.fda.gov/cdrhwebinar](http://www.fda.gov/cdrhwebinar). Again, thank you for participating. And this concludes today's virtual town hall.