FDA Virtual Town Hall Series – Immediately in Effect Guidance on Coronavirus (COVID-19) Diagnostic Tests

Moderator: Irene Aihie
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12:15 pm ET

Coordinator: Welcome, and thank you for standing by. At this time, all participants are in a listen-only mode. At the end of today's presentation, we will conduct a question-and-answer session. To ask a question, please press Star 1. Today's conference is being recorded. If you have any objections, you may disconnect at this time.

I would now like to turn the meeting over to Irene Aihie. You may begin.

Irene Aihie: Thank you. Hello. I'm Irene Aihie of CDRH's Office of Communication and Education. Welcome to the FDA's 46th 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 Timothy Stenzel, Director of the Office of in Vitro Diagnostics and Radiological Health in the Office of Product Evaluation and Quality, both from CDRH, will provide a brief update.

Following opening remarks, we will open the line for your questions related to the 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: Thanks, Irene. Thanks, everyone, for joining us again this week. I have a couple of updates from last week. The first is an authorization that went out on Friday for the Cue COVID-19 test for home and over-the-counter use. And this is the first molecular at-home over-the-counter non-prescription based tests that we've authorized.

And this is, excuse me - Cue did have a test that was authorized for point-of-care use already. And now this is their over-the-counter version that was authorized on Friday. And then also on Friday, authorized the first test for an adaptive T-cell immune response. This is the adaptive technologies to detect COVID test, which is NGS-based to aid in identifying individuals with an adaptive T-solver immune response to SARS CoV-2.

So, both of those authorizations have been posted on our website, along with other recent authorizations, and there was also a press release issued for each of those that you can find on our website. And I'll turn it over to Tim for his updates.

Dr. Timothy Stenzel: Yes. A pleasure to join all of you again today. Thanks for all that you're doing. We want to help you and speed access to additional diagnostics. So to - you know, we again, emphasize our priorities in particular home tests, is very, very important for us right now, either prescription or over-the-counter, whatever developers choose to come in with.

I do have a suggestion. It's just a suggestion, not a recommendation, but if you are developing a test that you envision can perform in the home, if you go straight to the home study, and don't do point-of-care studies, if we're able to authorize based on the home studies, you automatically get the point-of-care authorization as well.

So that is probably going to be a more efficient pathway, if you have high confidence in your test to be able to perform in the home, and you're ultimately going there, you cut out all those point-of-care studies, and you go right to the home user.

I also suggest, not necessarily recommend, because there is some risk to this, is that when you do the home clinical studies, that you overlap with that the same participants' usability study, user comprehension, with the clinical study.

So that will potentially make it a lot more efficient, fewer patients to enroll in your overall studies, you combine all those things. Don't forget the flex studies that are called for point-of-care. Those are also needed for home. And - yes.

And so, you know, to get into the home, it just requires adequate performance on 30 symptomatic patients, and that would be for a prescription. And then for over-the-counter, we'd like to see a minimum of 10 asymptomatic positives. And then any additional asymptomatic positives that we'd like to see, can be obtained post authorization.

So again, you know, we'd really like to see more home applications, either for a prescription or over-the-counter. And if it is more efficient for you to

bypass the point-of-care studies in CLIA waived clinics, that works for us as well. Okay. I think we're ready to go into the questions. Thank you so much.

Coordinator: Thank you. We will now begin the question-and-answer session. If you would like to ask a question, please press Star 1, please unmute your phone, and record your first and last name clearly when prompted. Your name is required to introduce your question. To withdraw your question, you may press Star 2. Once again, at this time, if you would like to ask a question, please press Star 1. And our first question is from Shannon Clark. Your line is open.

Shannon Clark: Good morning. This is Shannon Clark with UserWise Consulting. I have a question about prioritization of submissions. So, first of all, does the FDA prioritize US-made tests and over OUS-made tests? And also when submitting a low throughput CLIA antigen test kit with the intention of eventually getting into OTC, when could we expect to receive a response? Is that a matter of weeks or months or never? Yes. That's the question.

Dr. Timothy Stenzel: What is - the second question, can you repeat the second question? I didn't quite catch it.

Shannon Clark: Well, I know you're deprioritizing low throughput antigen tests or low throughput test kits. They're solutions that would only be using CLIA settings like H&M CLIA settings. So, when submitting something like that with the intent of getting into OTC and home use, when could we expect to receive a response? Is this such a low priority that we would not receive a response, or would we eventually receive a response?

Dr. Timothy Stenzel: I think what you're asking, and I just want to clarify, that if you submit, you know, a serology or antigen lateral flow test, and it's …

Shannon Clark: Yes.

Dr. Timothy Stenzel: And you only submit it for high moderate complexity, that is a very low priority and you might be deprioritized. We want to see at least point-of-care. But I'm suggesting on this call today that you just go to the home study. You save a lot of time and effort if your test performs there.

Shannon Clark: Though it does give management a lot more confidence if we can put a stake in the ground and get something, some sort of preliminary approval before investing in the very expensive studies to pursue home use. But my basic question is, what - is there some timeline in which we should expect to hear back from the FDA? Like, is it weeks or two weeks, or just kind of it'll sit there for months or?

Dr. Timothy Stenzel: So, we - so the antigen tests that are in for EUA, most of them have been submitted. They're still there, have been submitted this year, and most of them within the last few weeks. So, we are working through that, and we've done a good - a reasonable job in last - end of last year and into this year, but we have more work to do.

If we get a point-of-care study antigen test, or we get a home antigen test, that automatically takes priority over a higher moderate complex test. You know, if you've got data that you can - that have done - that you've followed our recommendations and templates, and you've got essay, you can - we have allowed then samples for higher and moderate complexity designations.

If your performance on those samples is 80% or above according to our recommendations, and you followed our other recommendations, you know, you have a device that works, so you've already eliminated the risk. We're not

going to raise the 80% for point-of-care or home RX. It's - that's where it stands and that's where it's going to stay. So …

Shannon Clark: That's great. I know you've heard I think …

Dr. Timothy Stenzel: As far as US versus OUS, no, it doesn't matter where the test is coming from.

Shannon Clark: Thank you. Excellent. Thanks so much.

Coordinator: Our next question is from (Chris). Your line is open

(Chris): Hi, Tim. I was wondering, we have not seen any recent postings of the FDA standard for molecular tests on the website. I was wondering, that has not been updated since I think October, and I had a client who got an EUA authorization in January, and they were wondering when they might see that data posted on the website.

Dr. Timothy Stenzel: So we are working on the next update, and it hasn't been - a target date hasn't been formalized yet. So all I can say is, stay tuned. We want to update it again as soon as we can.

(Chris): All right. Thank you.

Toby Lowe: Can you also clarify, did you say that you're asking about a test that was authorized in January, but you're not seeing that test posted on our website?

(Chris): No. I'm sending the results from the FDA panel.

Toby Lowe: Ah, okay. Thank you.

(Chris): It was not posted yet, but it's in the IFQ, of course, which we appreciate, but we were wondering about the posting. That was all. All right.

Toby Lowe: Thank you for clarifying

(Chris): Perfect.

Coordinator: Our next question is from Richard Montagna. Your line is open.

Richard Montagna: Thanks for taking a call. We are considering making some tweaks to our currently authorized tests to shorten the essay time. There would be no changes to the hardware of the disposables, but I have two quick questions. First one is, given CDRH's current workload, would such an EUA amendment request be reviewed?

And secondly, if so, we were planning to essentially just repeat all of the original studies for both the respiratory specimens that were in the original EUA, and then a subsequent amendment that we got authorization to include saliva, you know, things like confirming LODs, inclusivity, cross-reactivity or appearance, clinical data, et cetera, et cetera. So, that's the two quick questions.

Dr. Timothy Stenzel: So yes, that sounds like the validation we'd like to see. Can you tell me, is this a point-of-care home test?

Richard Montagna: It is a test for CLIA labs, high complexity CLIA labs.

Dr. Timothy Stenzel: High complexity CLIA labs. Okay. So, you can do your validation and submit the supplement to the FDA. And as soon as you submit it, you can launch your update while we review.

Richard Montagna: Thank you very much. Okay. That's great. Thank you very much.

Dr. Timothy Stenzel: You're welcome.

Coordinator: Our next question is from Raymond Boulay. Your line is open.

Raymond Boulay: Yes, good afternoon, Tim. We see that several manufacturers are offering COVID-19 collection kits through e-commerce platforms such as Amazon. And with OTC tests coming along, we're anticipating that this business model may also be used for distribution of OTC COVID-19 tests, not just collection kits.

Current conditions for authorization require manufacturers and distributors to have systems in place for collection and reporting of complaints, as well as reporting a false positive and false negative results. Isn't FDA's expectation that Amazon or other e-commerce sales engines, would be required to comply with all the requirements of authorized distributors? Or would that fall to - or could that fall exclusively to the manufacturer via some arrangement with the e-commerce platform?

Dr. Timothy Stenzel: So, if you had an agreement with Amazon or any other distributor of e-commerce or otherwise, to have the manufacturer handle the complaints and have a system funnel those complaints into that manufacturer, that works just fine.

You can also, in the labeling of the product, provide information to the

consumer about how they can reach the company for complaints and or the Med Notch program. Toby, do you have anything else to add?

Toby Lowe: I would just clarify that, you know, the - if Amazon or another e-commerce site is acting as a distributor, they are responsible for meeting the conditions of authorization for a distributor. How they go about meeting those is - you know, as Tim said, can be through an agreement with the manufacturer for who's doing what.

Raymond Boulay: Okay, great. Thank you very much.

Dr. Timothy Stenzel: You're welcome.

Coordinator: Our next question is from Jo-Ann Gonzalez. Your line is open.

Jo-Ann Gonzalez: Hi. Thank you for taking my questions. For an antigen OTC test where results are determined with a cellphone app, I understand that enrichment is permitted for asymptomatic subjects. As overall prevalence rates continue to fall in the US, is the FDA receptive to enrichment for symptomatic subjects?

For example, if a symptomatic person tested positive and was still within seven or 10 days of symptom onset, would it be acceptable to enroll that known positive in the study?

Dr. Timothy Stenzel: Yes. The short answer is yes. We understand that some of the positivity rates are falling. We will accept, you know, unbiased enrichment strategies. We do recommend you run by - that enrichment strategy by the FDA to mitigate any risk of your study plans.

Dr. Timothy Stenzel: Okay, thank you.

Coordinator: Our next question is from Ron Domingo. Your line is open.

Ron Domingo: Hello. Thanks for taking my call. If a company has achieved an EUA for symptomatic claim, the antigen template allows for adding a asymptomatic claim by testing at least 100 negative and 20 asymptomatic positives. Can such a study be performed in a nonclinical setting such as in an employer testing site?

Dr. Timothy Stenzel: So, that's - you're going for an OTC claim, right?

Ron Domingo: Yes.

Dr. Timothy Stenzel: Right. So first of all, we're currently authorizing OTC tests that already have a home prescription authorization, with 10 positive asymptomatic samples. So not 20. So, 10 on positive pre-authorization. We would ask you that anything less than 20 be made up after authorization.

We would also like to see, for those 10 asymptomatic positive samples matched - symptomatic samples matched to the OTCs in that - in the asymptomatic population. So, you know, find match samples to that, which should be easier to get.

And then in order to get those positive asymptomatics, we do allow enrichment. So, you can connect with a surveillance or screening program, as long as you do the subsequent testing in an unbiased way. So, getting the positives in asymptomatic situation is what we hear is more challenging than getting, you know, 100 negatives, which is pretty easy to get.

And you can do that testing, either you can send it to the home user and they

can do it entirely in their home, or you can set up simulated environments, and if you want to use schools or workplaces to enroll people, as long as you simulate how a home user would use that when you hand them over the test, that works for us.

Ron Domingo: Okay. Thank you Tim.

Coordinator: Our next question is from (Anna) (inaudible). Your line is open.

(Anna): Hi. Good eve - it's evening here in Israel anyways. So, we're developing point-of-care breath test, and I want to ask if you can make a clarification. So, if a test is known to be performed at point-of-care by trained people, trained personnel, but not medical professionals like nurses or doctors, it could be formed by a medic or by anyone who went through a certain training, so is it considered OTC or by - or for prescription use?

Dr. Timothy Stenzel: Yes. so, for point-of-care tests to be performed in CLIA waived settings, also can - anything that we deem point-of-care and can be used in waived settings, can also use - in moderate or high complexity labs, but they're not considered over-the-counter. They would only be to a consumer in a home situation.

When you do your point-of-care studies for your device -- and good evening to you in Israel -- we ask that you use true US equivalent of point-of-care sites with equivalent personnel. So, no trained laboratorians is one of the key features, but, you know, anybody in a typical physician office practice situation, the physician nurse, allied health professionals, are the types of people who haven't been trained formally in laboratory medicine.

And so, that's the untrained healthcare workers we're talking about. Did that address your question?

(Anna): So then that would still be considered for prescription? I mean, a physician would still have to prescribe, you know, or ask for the test to be done?

Dr. Timothy Stenzel: Yes.

(Anna): This is meant for a workspace setting, for example, or for a school?

Dr. Timothy Stenzel: Right. So, in the setting - a school setting, that would still be considered a prescription device. We are - the FDA signaled that we're open to blanket prescriptions, you know, and follow up with State or local law. But a given institution can have one physician prescribe it for that institution, one prescription.

And of course, that would be - those institutions would have a CLIA waiver certificate to do that - the clinical testing in that setting, and they would have reporting requirements.

(Anna): Thank you.

Coordinator: Our next question is from (Franklin Codron). Your line is open.

(Franklin Codron): Good afternoon. Thank you again for doing this, and for taking questions. My question is related to the Ellume test, to the Quidel QuickVue At-Home COVID-19 test. The Ellume test is supposed to be 100% self-used at home, no prescription. However, you can correct me if I'm mistaken. I have not

seen the test being sold or marketed yet. I have heard that the issue may be related to the reporting component of the test.

And on the second one, I noticed Quidel decided, on the reporting part, to leave it up to the consumer to report it to their healthcare provider. What I'm guessing is that there are some issues or maybe some high bars related to the reporting of results. I don't know exactly what those are.

I wonder if you can speak to some of that, because we - you know, the window of opportunity for our tests, for the antigen test for COVID done at home, is shrinking, right? Yes, you know, we still have to vaccinate a lot of people, but in realistic terms, you know, the window keeps shrinking.

So we want to stay realistic with this project. We have been at it since last August, and we're still unable to complete. So, are you able to provide any light as to, you know, why to date, we don't have a 100% COVID at-home test available that we can actually buy? Maybe you can provide some tips on how to get around maybe this difficulty.

And by the way, I did connect with some of the folks that are part of the design-a-thon, and they don't seem have the guidelines very clear as to what FDA wants on the reporting component for an at-home self-test, antigen test. I wonder if you could provide some guidance on that as well, so maybe we can connect the two parts and get something going.

Dr. Timothy Stenzel: Sure. So, I'll just be very clear. The law does not require home testing to be reported, and the FDA does not require reporting at the time of authorization. We are encouraging all developers to have a plan for reporting because it does not - it's not a requirement, but is very useful to healthcare authorities to monitor the pandemic.

So, that's - somewhere, this notion got out there that we require reporting for OTC or any home testing, and that's absolutely not true. We will authorize, as we did the Quidel home test, without a reporting feature. We encourage all developers though to subsequently develop something, but it's not something that we would turn down an application for.

And then as far as commercialization of tests that have been authorized, that's entirely up to the developers. That's not an FDA position, and we would never hold up commercialization into the home because of there not being a reporting function.

We want to get these tests into the home as soon as possible. We encourage developers to develop a reporting feature that's always pre-market or unconnected.

(Franklin Codron): Okay. Just a couple of things there. On the Quidel test, their IAC does say that the user should report the results to their healthcare providers. So, you know, I don't know what that means. And on the second point about FDA not preventing the commercial aspects of the test, I understand that 100%.

However, it is a little - I'm a little curious as to why to this day, we still don't have a 100% health use at-home test that, you know, the user can go all the way without having to report to anybody. Maybe I'm missing something there, right?

Dr. Timothy Stenzel: So, the tests - the home tests that have a reporting feature now, other than the BinaxNOW, which has a telehealth component, the users are not required to report. They can opt out of reporting

(Franklin Codron): I see. Okay. And then on the - yes, okay. Thank you for that clarification. And then on the last point about the design-a-thon with HHS, which I mentioned that I was able to connect with some folks that are working with solutions there, I had a couple of conversations with a couple of companies, but it does not seem like they understand exactly what FDA is requiring on that reporting part.

So, do you foresee providing any guidance that maybe we can share with those folks, if we do decide that we want to add the reporting component, because we do see the value in reporting this to public health?

Dr. Timothy Stenzel: So they're there to help you come up with a reporting function. They're not there to make an FDA decision on whether to authorize it or not. And it may be very encouraging of using a reporting feature at the time of authorization, but they don't have - they don't - they have not imposed that requirement on us. It isn't imposed by law.

So, if they - and if you're working with them on a reporting feature, you know, the one thing is, if they're asking you - if they're making it mandatory for all patients to report, that would be something that I'd be willing to help have a discussion. But the other thing, it's normally up to the FDA who we authorize, not to those folks.

(Franklin Codron): Okay. Thanks for that.

Coordinator: Our next question is from (inaudible). Your line is open.

Man 1: Good afternoon. Thank you for taking the question. I am (inaudible) from (inaudible). I have a request to Tim and Toby. It's really very nice to have

these calls, and it is very useful. Only my thing is, the transcript of presentation takes almost 10 days to be posted.

So, it will be nice if the transcript can be posted the same week, at least before the next call, so that we know what had transpired in the previous call. It is really important the information is communicated to the community in a timely manner, especially people who have not attended the call.

Last time, you know, we had some issues in the call, and we did not get all the information. We have to wait till next Friday or I don't know, this Friday to know what really had happened. So I really request and appreciate if some additional resources are made so that the transcript and presentation is posted earlier than what is done right now. Thank you.

Toby Lowe: Thanks for that feedback. You know, I think we do appreciate your feedback on that, and we do understand the desire to get this information as quickly as possible. Most of the timing is out of our hands. You know, we do have to wait for the recording and the transcripts to come to us before we can get those posted. But we will relay that feedback and see what can be done.

Dr. Timothy Stenzel: You know, we typically don't get the transcript back until the Monday following. And then we go over it to make sure it's clear. So, we'll take that back into (inaudible).

Man 1: (Inaudible) record the electronic and it should be done very fast.

Toby Lowe: We'll take our next question.

Dr. Timothy Stenzel: Yes. Thanks.

Coordinator: My next question is from Raymond Brewer. Your line is now open.

Raymond Brewer: Yes. Hello again, Tim. For an antigen over-the-counter test that incorporates a smartphone application that reads the test, if the manufacturer conducts their clinical study to support your EUA for an OTC claim, and at the conclusion of the study, they don't meet OTC PPA requirements, but they do meet prescription-only requirements and they submit that, and if we're - if FDA were ultimately to authorize that down the road post-authorization, if the manufacturer made an improvement to the analysis algorithm, that results in an increase in the PPA that would actually meet OTC requirements, would the test developer need to fully repeat the clinical study to pursue that OTC claim, or could they use the original clinical data and rerun it through the new algorithm?

Dr. Timothy Stenzel: It depends. If you use the original clinical study data to train the new algorithm, then it would be just matching the test results. If you use an independent set to train your system, then you can use that original dataset to validate.

So the thing is, when someone comes in for an original authorization or any supplement or amendment, they can ask for - they can propose a pre-approved change protocol, which would spell all the science, and it makes us easier to get the update to your test. So we're open on all those accounts.

So, the other thing is, when we look at the OTC situation with a submission for home, you know, and sometimes, you know, we want to look at all the data. So, you know, if you have a test that's functioning well and, you know, symptomatics are at least 80% or above, we want to look at the totality of the evidence in making the OTC decision.

Our recommended level for OTC is 90%, but that's just what I've said as a recommendation. So if - you know, I'd encourage you to - the other thing is, if you have a performance that works for a prescription right now at home, I would suggest you send that in to us now and have us go ahead and have that discussion now with you.

The other thing about prescription home use is, maybe surprising to some, but I have heard that there's quite a bit of interest in home use prescription tests. So, I don't think there - I think there's - my yeo cents is that there is a market for prescription home, a big market for prescription home use tests right now.

Raymond Brewer: Okay, great. Thank you very much.

Dr. Timothy Stenzel: You're welcome.

Coordinator: And at this time, I'm showing no further questions.

Irene Aihie: Tim and Toby, before I close out, did you have any further closing remarks?

Toby Lowe: I did want …

Dr. Timothy Stenzel: I don't. I am going to drop off though, because I do have another meeting I need to run to and Toby is going to take over from here.

Toby Lowe: Great. Thanks, Tim. I did want to add one clarification to the breath test discussion from a little bit earlier in this call. Just to clarify, you know, we don't want to speak for CMS, and you should always check with CMS on the clear regulations. But our understanding is that breath tests may not be covered under CLIA.

So that is something to take into consideration when you're, you know, considering the setting in which you are intending your test, and we would want to make sure that the validation data that you provide is suitable for the setting in which you're intending for your test to be performed, which may be in a CLIA lab. It just may not fall under the - under CLIA, the way that other tests may.

Irene Aihie: Thanks, Toby. Brandon, do we have any other callers in the queue?

Coordinator: Looks like we do have one more question in the queue. One moment, please. All right. Our question is from Shannon. Your line is open.

Shannon Clark: Hello. This is Shannon Clark with UserWise Consulting. For designing a point-of-care study, can I design it to exclusively rely on retrospective clinical specimen, such that the minimally trained operators are not doing any sample collections, they're just using leftover specimens in VTM randomized between positive and negative?

Toby Lowe: Sorry. I missed the beginning of that, I believe. What type of study are you asking if you can use retrospectives?

Shannon Clark: For an antigen test kit point-of-care study with minimally trained HCP operators.

Toby Lowe: So that might be something that we would need to see your study design. I'm not sure how that would be managed, since most of those point-of-care tests would involve collection and immediate testing.

Shannon Clark: Because the template says, it may be acceptable to use retrospective clinical specimens. So I guess my impression is, you probably want some live collection happening, but then you could augment the symptomatic positive specimens by having some retrospective leftover specimens in DTM. Is that a proper read inference from that sentence?

Toby Lowe: I think it would depend on the design of the test and the design of the study. So we would want to see some more details on that before we could weigh in on that.

Shannon Clark: Okay. Thank you.

Irene Aihie: Brandon, do we have any other questions?

I'm showing no further questions at this time.

Irene Aihie: Thank you. Again, this is Irene Aihie. We appreciate your participation and thoughtful questions during today's town hall. Today's presentation and transcript will be made available on the CDRH learn webpage at www.fda.gov/training/CDRHlearn by Friday, March 19th.

If you have additional questions about today's presentation, please email 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. This survey can be found now on www.fda.gov/CDRHwebinar. Again, thank you for participating, and this concludes today's town hall.

Coordinator: Thank you for participating in today's conference. All lines may disconnect at this time.

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