

NWX-FDA OC

Moderator: Irene Aihie
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Coordinator: Hello and thank you for standing by. At this time I'd like to inform all participants that today's call is being recorded. If you have any objections you may disconnect at this time. You have been placed in listen-only mode until the question-and-answer session of today's call. At that time we are taking calls over the phone only. And if you would like to ask a question please press Star 1 and please make sure that your phone is unmuted and record your name clearly when prompted so I may announce you for your question. Thank you and you may begin with your host Ms. Irene Aihie.

Irene Aihie: Hello and welcome to today's FDA webinar. I am Irene Aihie of CDRH's Office of Communication and Education. On February 29, the FDA issued the immediately in effect guidance titled Policy for Diagnostics Testing in Laboratories Certified to Perform High Complexity Testing Under CLIA prior to Emergency Use Authorization for Coronavirus Disease 2019 during the Public Health Emergency.

This guidance provides a policy for novel coronavirus molecular diagnostic tests developed and used in laboratories certified to perform high complexity

testing under the Clinical Laboratory Improvement Amendments prior to issuance of emergency use authorizations for such tests.

Today Timothy Stenzel, Director in the Office of In Vitro Diagnostic and Radiologic Health in the Office of Product Evaluation and Quality here in CDRH will present an overview of the guidance document. Following the presentation we will open the line for your questions related to information provided during the presentation.

Additionally there are other center subject matter experts here with us today to assist with the Q&A portion of our webinar. Now I give you Timothy.

Timothy Stenzel: Welcome. It's great to share this new policy with you today. This policy is for diagnostic testing, in laboratories certified to perform high complexity testing under CLIA, prior to EUA authorization. The agenda today will be to go through the background summary of the immediately in effect guidance and then of course take questions and provide some answers.

The objective today is to explain this new policy for molecular diagnostic testing and high complexity Clinical Laboratory Improvement Amendments (CLIA) certified labs prior to emergency use authorization for coronavirus disease 2019 and now the coronavirus during this public health emergency.

Some background. This guidance was issued on February 29, 2020. It describes a policy regarding certain laboratories immediately using tests they have developed and validated in order to achieve a more rapid testing capacity in the United States.

With the COVID-19 public health emergency the FDA has determined that prior public participation for this guidance is not feasible or appropriate. And

issued this guidance without prior public comment. This guidance document is immediately in effect but remains subject to comment in accordance with the FDA's good guidance practices.

Scope. This policy is limited to laboratories certified to perform high complexity testing consistent with the requirements under the clinical laboratory improvement amendment and is for molecular diagnostics for the SARS-COV-2 virus. The new policy does not impact requirements under CLIA, does not impact CDC recommendations for who should be tested.

Policy. The guidance includes recommendations regarding validating newly developed coronavirus tests prior to clinical use, notifying the FDA when clinical use of a validated test begins, confirming the first five positive and negative samples with EUA authorized tests, indicating in test reports that the test has been validated but independent review by the FDA is not complete, submitting EUA within 15 days of initiating testing and, finally, steps to take if any specimen fails confirmatory testing or if the FDA is unable to authorize the EUA.

Test validation. The guidance includes recommendations regarding the minimal testing to be performed for validation. These include Limit of Detection or LOD, clinical evaluation, inclusivity, cross reactivity. And then comments on the limited viral materials that are available to the FDA, BARDA, and the CDC of prioritized and coordinated shipments to labs when ready to validate.

You can address this by sending an email to the FDA email as listed later in this presentation. This is limit of detection testing under this guidance defined as the lowest concentration in which at least 19 of 20 replicates are positive. The methods include we recommend testing dilution series with three

replicates at each concentration in order to find the range of the LOD for your assay. And then when you have done this confirm the final concentration with 20 replicates. And this is – and do these 20 replicates after you've initially identified the LOD. And again 19 of these 20 replicates at least – so 19 or 20 are to be positive to pass this limit of detection criteria.

The samples they can be pooled negative clinical samples or artificial matrix. If multiple specimen types are included the most challenging of these should be evaluated, for example sputum. This slide describes the recommended clinical evaluation testing. At least 30 contrived reactive specimens and 30 non-reactive specimens should be tested. The contrived reactive specimens can be created by spiking in viral RNA or an activated virus into leftover clinical specimens.

Twenty of these contrived specimens should be spiked at a concentration of between 1X and 2X of your determined LOD for your assay with the remainder of the specimen spanning in the assay testing range. Acceptable performance for this clinical evaluation is 95% agreement at the 1 to 2X of LOD.

So again that means 19 or 20 positives out of those near LOD samples. And then 100% agreement for all concentrations that are above the 1 to 2X LOD and for all negative samples.

Inclusivity testing recommendations. Inclusivity can be conducted with in silico analysis of the percent identity matches against publicly available novel coronavirus sequences that can be detected by the proposed and developed molecular assay. One hundred percent of published sequences should be detectable with the selected primers and probes for your assay.

Cross reactivity testing is recommended that you conduct an in silico analysis of the assay primer and probes compared to common respiratory flora and other viral pathogens. There should be greater than 80% homology between one of the primers and probes and any sequence present in the targeted microorganism.

It is recommended that you follow recognized laboratory procedures for any additional cross reactivity testing in the context of the sample types intended for testing.

I wanted to give you an update of the EUA tests. First of course the CDC was given an EUA authorization on February 4 for their tests and their kits. This also under the CDCs EUA there is another covered test and that is the IDT 2019 novel coronavirus kit. We are doing a lot of qualification tests. The CDC rather is doing a lot of qualification testing. And the lot that is already passed from a QC at the CDC is Lot No. 000500383.

If you are a laboratory that has this kit lot and can use it according to federal, local and state laws and regulations, you can go ahead upon verification that you normally perform when you receive a kit. You can go ahead and begin clinical testing on this lot. Stay tuned as additional IDT lots are undergoing qualification by the CDC and that information will be made known publicly as soon as possible.

In addition you may have noted that the FDA has issued a second EUA authorization for New York State Wadsworth Center on February 29, 2020.

And finally, the CDC, FDA and BARDA are working with multiple IVD manufacturers and laboratories to enable additional EUA authorizations as soon as possible. You can monitor this at our Web site. We will post all new

EUA authorizations as soon as those authorizations occur. So you can keep track of this.

How do you perform your submissions to the FDA? First of all once you have validated your assay according to these recommendations and met the performance criteria, laid out in this webinar and in our guidance, you can begin testing as soon as you notify us of that. Your notification can be sent to this email address – CDRH-EUA-templates@fda.hhs.gov. Include the name of your laboratory, the name of the laboratory director, your address and a contact person.

This is also the same email that you can use to ask any inquiries of this process. Request through the FDA, BARDA and CDC access to viral RNA for virus that is currently being managed by a number of entities. The EUA should be submitted then. That is the completed package 15 days after your initiating clinical testing. And you can send that to the email address here – OIR-operations@fda.hhs.gov. And should include the following information on these forms and the completed EUA template.

I should back up and say that upon submission of a notification to the notification email we will receive a response back. You should receive a response back and if you haven't please contact us so that we have received that notification email.

Finally I think is the last slide. Here are some resources that you can utilize in this process for the COVID-19 guidance, general EUA guidance documents and FDA's novel coronavirus Webpage. I would like to also relay an important announcement that some of our public health lab officials have asked that we do. I am just pulling up that email right now – is the delay.

This concerns public health reporting. And I think we're all in the same boat here and we really encourage you to help us out in meeting this emergency need. We strongly encourage laboratories seeking testing under this policy to contact their state public health department as early as possible in the process. Perhaps even before receipt of any orders or samples to help ensure they have capacity for the validation testing described in the guidance and have the information necessary to support case investigations. We also encourage laboratories to be sure they are familiar with state and local laws maintaining reporting of diseases and conditions of public health significance. And that ends that statement that we wanted to make.

So for any questions you can address them to this email address – CDRH-eua-templates@fda.hhs.gov or call us at 301-348-1778. To receive the slide presentation transcript and webinar recordings you can go to this link which will be up shortly after this webinar. And with that I believe we'll open up for questions.

Coordinator: Thank you. It is now time for the question and answer session of today's call. Again if you would like to ask a question over the phone please press Star 1. Please make sure that your phone is unmuted and record your name when prompted. If you wish to withdraw your question you may press Star 2. Thank you, please give a second for me to get the names. First question comes from (Pamela Martiniak) your line is open.

(Pamela Martiniak): Hi. I'd like to know if there's any recommendations or guidance on the procedure codes that will need to be used to bill for the testing and, you know, if there are any out there that are specific to the kits that you mentioned.

Timothy Stenzel: That's an excellent question. That would not be under FDA's purview. I would suggest that you reach out to CMS to get a response for that.

(Pamela Martiniak): Thank you.

Coordinator: Thank you. Next question comes from (Richard Montegna) your line is open.

(Richard Montegna): Yes thank you. I noticed that in the EUA template the contrived samples numbered 50 either 50 contrived or 50 clinical and in this webinar you just mentioned 30. So has that number changed or is this only for CLIA labs because we're an IVD manufacturer?

(Uwe Scherf): Yes, this is (Uwe) from Division of Microbiology Devices. Yes this number has changed in order to address the validation challenges associating with verifying devices – yes going forward the number of samples have been reduced.

(Richard Montegna): Okay thank you. And related to that we are trying to establish the limit of detection. And we have been working with Zeptomatrix in Buffalo who frequently is able to get these viral samples from CDC or others. And as of right now BEI Resources is shipping only to BSL3 labs and not allowing them to reship inactivated viruses. So that's make it a little difficult for those of us in the industry because we have BSL2 labs but not BSL3 labs. So, my question is is there anything being done to address that or secondly it looks, like we might be able to use viral RNA that I understand is now available to set LODs.

Timothy Stenzel: Yes. So you can request viral RNA if you're not a BSL3 facility who can handle live virus. And right now you can request that from BEI and UTMB. Now there is currently a limitation on the availability. And if you are requesting that you have access to that if you have any issues in ordering that

from those two entities, please send us an email to CDRH-EUA-templates@fda.hhs.gov and we will work with you.

(Richard Montegna): Okay.

Timothy Stenzel: Also the procedures for validation in this new guidance are suggestions and recommendations. If you have ideas for alternative approaches, please reach out to that same email and we will work with you in cases such as this where you cannot easily access viral isolates or viral RNA.

(Richard Montegna): Okay thank you very much, appreciate the help.

Coordinator: Thank you. Next question comes from (Ali Nori). Your line is open sir.

(Ali Nori): Thank you very much. Just a quick question. I'm wondering if you can tell us, you know, anything as to which of the reagents was the problematic one in the initial kits issued by CDC. There's some report suggesting they were the primers in the N3 reaction. There's other reports suggesting it was something that was creating false positives. I'm just wondering if you can sort of elucidate some of that.

Timothy Stenzel: Sure this is what I can tell you that we believe that the design of the original CDC assay that was reviewed under the EUA application is solid. We have a lot of confidence in that. And that includes the N1, N2 and N3 and the control reaction – the RP control reaction.

And as regard to CDC assay we have worked closely with them. And we believe we have resolved the manufacturing issues. And so now kits are again being shipped to public health labs. And as I mentioned earlier we are working with more than one manufacturer. But the one we can publicly

announce today is IDT. And we have a process to qualify those lots. And as soon as lots are available our laboratories can contact IDT and purchase those kits for their uses.

If you purchase those kits under IDT that have been lot qualified, you will not need to submit your own EUA. That's the beauty of this approach. You can simply do the normal verification testing upon receiving a new kit as if it's another EUA authorized kit.

(Ali Nori): So the primer sequences are the same then.

Timothy Stenzel: The primer sequence in the IDT reaction are exactly the same as the CDC primers yes. And the IDT kit includes N1, N2, N3 and the control reaction.

(Ali Nori): So was it just a bad lot initially? Was that creating the problem the design was good but there was something wrong with one of the lots?

Timothy Stenzel: The design is good. It was a manufacturing issue that we have now resolved. That we have resolved I should say in conjunction with the CDC resolve and the FDA did provide assistance in that.

Coordinator: Okay thank you. Next question comes from Dr. (Manad Salem). Your line is open.

Dr. (Manad Salem): Hi thank you so much for the great presentation. I just have a general question about notifying FDA for clinical use of laboratory developed tests. Is it included for every laboratory developed test or is it specifically for the SARS COV coronavirus detection?

Timothy Stenzel: No this new policy was only for the novel coronavirus. However I will add that your design does not need to be the CDC's design. It can be whatever design you choose as long as it's properly validated.

Dr. (Manad Salem): Thank you so much.

Coordinator: Thank you. Next question comes from (Arthur Kowaski). Your line is open. (Kawasaki) sorry.

(Arthur Kawasaki): Thank you. I just have two questions. One, I would like to confirm the notification when starting initial clinical studies is not required if an industry member is already engaged in FDA and the Pre-EUA, EUA interactive review. And the second question is regarding the EUA proposals for any differences or deviations from the policy or guidance that does not have to be notified as it will be done under interactive review if an industry member has initiated that.

Timothy Stenzel: So are you in a CLIA-certified high complexity laboratory?

(Arthur Kawasaki): No not specifically. We're just an industry member and we actually haven't engaged FDA are thinking of engaging FDA with the Pre-EUA, EUA interactive review.

Timothy Stenzel: Okay you can submit inquiries to the same email address and we will work closely with you, interactively with you to assist you in any way we can with validating your assay under the EUA provisions.

(Arthur Kawasaki): Okay, thank you.

Coordinator: Thank you. Next question comes from (Ali Burken). Your line is open.

(Ali Burken): Hello. I was wondering how does the FDA guidance impact test kit manufacturers who wish to immediately sell a test kit to hospitals or airports, you know, for detecting the coronavirus?

Timothy Stenzel: So under this guidance high complexity, CLIA labs can purchase RUO components and validate them according to these recommendations. And once that has happened you can notify us and begin testing. That is at the moment under this policy – that is under this policy what can be done with manufactured reagents. Also if you're a CLIA certified high complexity lab you can develop your own reagents and follow the guidance.

(Ali Burken): Yes I understand that. At that point we can begin testing after validation and notification. But I'm talking about in terms of selling a kit to third parties to allow them to perform the testing.

Timothy Stenzel: Again test developers can purchase RUO reagents for their test development purposes. Manufacturers if they want to distribute their kits will still need to be coming through the EUA process. Please email us at cdrh-eua-templates and we will work through it with you in order for you to achieve that EUA authorization.

(Ali Burken): All right thank you very much.

Coordinator: Thank you. Next question comes from (Douglas Shanay). Your line is open. Can you check the mute function on your phone please? Okay next question comes from (Nahed Mosin). Your line is open.

(Nahed Mosin): Yes hello. This is (Nahed Mosin). I just have a question for you. After – so getting – while we're getting the EUA authorized assay application, we need

to evaluate, to do the clinical testing. The question that we have how are we – yes we are the manufacturer. We're not the clinical laboratory, high complexity clinical laboratory. So our question in order to validate that and confirm our assay, how are we going to get those positive clinical specimens or negative clinical specimens to do the clinical testing itself?

Timothy Stenzel: All right. So we understand that this material right now can be – in the U.S. can be limiting. You can send us an email request at cdrh-eua-templates@fda.hhs.gov. And we will add you to the list of entities that would like to obtain these materials. You can also work interactively with our staff in order to determine if there are alternate pathways that you can take to validate your assays.

(Nahed Mosin): Okay. The other question that we have if you don't mind. We have done our instrument. We have gotten approval for one instrument to other assays with FDA which is basically a PCR instrument. The question is we can go ahead and use other instruments as well?

Woman 1: No that instrument is also approved for LDTs use...

((Crosstalk))

(Nahed Mosin): Yes but it's not through FDA use, you know, it is not approved yet by FDA. Can we use those assays on these instruments?

Timothy Stenzel: So I would ask you to send some of these details to the cdrh-eua email address. And we will respond with – will ask for probably more details and will respond as quickly as we can which we are doing a great job right now in providing you specific information that is directly related to the instruments you're interested in.

(Nahed Mosin): Okay one more question. What's the timeline for approval estimated?

Timothy Stenzel: So once we have a complete package if you're an IVD test manufacturer we suggest that you start sending in portions of your submission under what's called the Pre-EUA process. That will allow us to have a rolling review of your information so that when you submit the final part of the application our assessment is at that time only going to review the final part. And that can happen relatively quickly. So say that for both the CDC and for the New York State EUA authorizations most of those were handled in a similar manner. And those final authorizations came within about 24 hours of the final submission being made.

Woman 1: Okay. So we are currently – have an assay developed, we use for nasopharyngeal swabs and nasal swabs, UGM transport medium. And if we want to because the difficulty is to secure some clinical sputum samples. Is it possible we can submit the first – just one use, one kind of matrix and follow up with the more expansion of the matrix?

Timothy Stenzel: No the EUA authorization is – it can absolutely be amended and updated over time. So again for specific questions for IVD manufacturers, I would recommend you send an email to the cdrh-eua. I would ask that traditional IVD manufacturers that they do this. This call is really to describe the policy for lab developed tests at CLIA high complexity labs. So I want to make sure that in the time allotted that I can address all of the CLIA lab questions.

(Nahed Mosin): Okay.

Woman 1: Okay, thank you.

Coordinator: Thank you. And please going forward please limit yourself to one question. If you would like to ask another question you can rejoin the queue. Thank you. Next question comes from (Breanna Sewell) your line is open.

(Breanna Sewell): Hi sorry. So we have a question regarding registration in the BEI. We are not currently registered but we want to be able to order some viral RNA. But does it makes sense for us to get a draft in order to send to you all to start the review process before worrying about registering to order the RNA or how do you suggest we handle that?

Timothy Stenzel: I would suggest you reach out right away to the email address and put that request in. If you have any questions about how you register we perhaps can help you. While in parallel you develop your plan or your validation if you have any questions about how you approach that. You can also send those email questions to us.

(Breanna Sewell): Okay yes I already did an email. I received an email back today with how to go ahead and register. That's why I was just wondering. I wasn't really clear which I should, you know, prioritize.

Timothy Stenzel: I would work on all things that you can at the same time in parallel.

(Breanna Sewell): Okay thank you.

Coordinator: Thank you. Next question comes from (Sevems Betha) your line is open. Please check the mute function on your phone. Next question comes from (Chen Zen) your line is open.

(Chen Zen): Yes my question is whether FDA's considering expanding the scope of EUA to non-molecular based tests for IVD matures in labs. If yes are you partnering

with manufacturers or labs to develop a template for non-molecular based tests?

Timothy Stenzel: Let me turn that over to Uwe if you could comment. I'm thinking that if it's a non-molecular test I think we'd want to know something more about it and the more traditional EUA process to start this off might be good by asking questions by sending emails to us. But I'll turn it over to Uwe to see if he has any comments.

(Uwe Scherf): I think you understand of course that the molecular approach has opportunities that other technologies will not offer. So I suggest that you work with us in the pre-EUA process to then describe to us what you are planning to do and we will provide you the appropriate feedback on the next steps. And again requests can be done with the email address that (Tim) mentioned those times already.

(Chen Zen): Yes we did send (Tim) an email, you know, giving them a description of the lysis. But the response we got is that you are still – your resources are strictly focusing on the molecular based tests. So it seems you're not ready to take non-molecular based tests. Is that true? Do you have a timeline that you can expand the scope to other tests?

(Uwe Scherf): Well we are working as fast as we can getting all of the requests done. But I cannot give you a specific timeline.

(Chen Zen): Okay.

(Uwe Scherf): But individuals here are trying to assure that all of the requests and all of the technologies can be supported the appropriate way.

Timothy Stenzel: And here the technology that you believe can be helpful in this situation either in the shorter term or the longer term, I would suggest that you continue to develop your product. And our team will get back to you as soon as they can. I do want to encourage all types of diagnostic development here.

(Chen Zen): Okay thank you.

Coordinator: Thank you. Next question comes from (David Perlin) your line is open.

(David Perlin): Oh hi thank you for this. I wanted to ask you about clinical CLIA lab, about a limit of detection and clinical specimens that you're recommending for the validation. In terms of limit of detection do you have a number in mind? Is it 10 particles genome, 100 for your limit of detection? And you mention sputum as well in clinical specimens. Are you also - are you looking at nasal washes, bronchial washes, sputum? Can you give a little more guidance on that?

(Uwe Scherf): Yes. I mean the sensitivity you can imagine that the performance needs to be evaluated towards that concept. And except viral load we will not be able to provide you with a number. But the material that you are spiking will have a certain concentration. And we would like to assure that the assay is sensitive enough for the performance. Regarding the specimen that you said again of course nasal washes and nasal pharyngeal washes are also specimens that clearly are needed for evaluation.

The concept here if you are limited with material and you want to really then also go into lower respiratory specimens that you could consider using that as the most challenging matrix that you are evaluating. Assuming then the other matrixes will be performing similarly and you can move forward with the testing.

Timothy Stenzel: As you begin your testing and you start to get results for what your LOD is that you think it may be, please don't hesitate to contact us at the email address and check in with us if you have any questions about...

(David Perlin): You know because we're doing spike in studies now and we're just trying to understand what sort of thresholds you're looking for for LOD.

Timothy Stenzel: Yes. So we're still very early in this process with this virus and this disease. And it is why we're focusing first on molecular techniques because at the moment we want very sensitive techniques to be able to detect the virus. So standard molecular detection LODs for viruses in nasopharyngeal and oropharyngeal specimens are, you know, in the range especially if you know anything about coronavirus in general that would be another place to start. (Uwe) do you have anything else to add to that?

Uwe Scherf: I think that captures it, yes.

Timothy Stenzel: Okay thank you.

Coordinator: Next question comes from (Kazi Masira) your line is open.

(Kazi Masira): Hi. I have a follow up question from the previous question regarding the LOD validation. So if you are doing the validation with wild RNA we are doing it BSL2 level. But once you have the samples and your patient samples you move back BSL3 level. Is my understanding correct?

Timothy Stenzel: You know I think that is a CLIA question as to what it is. Let me just check and see if we can provide any comment on that. So do check with CLIA but I

believe at that point BSL2 level testing is still appropriate. But please do check with CLIA.

(Kazi Masira): Okay thank you.

Coordinator: Thank you. Next question comes from (B.J. Dacall) your line is open.

(B.J. Dacall): Hello. We have a question about the IDT lots. Which ones are approved and where do we find that list of approved lots of IDT? And can you elaborate around that EUA that you authorized if we're buying an approved lot from IDT? We're good to start clinical testing without validation.

Timothy Stenzel: So if it's a lot that's been qualified by the CDC under their EUA authorization you do not need to submit your own EUA. We are still working on how we're going to make that information public. So stay tuned and stay in touch with IDT. At this moment that's what I recommend. They were expecting that they might receive some inquiries about this. And as of now we only have one kit left to announce but again stay tuned.

(B.J. Dacall): Thank you.

Timothy Stenzel: Let me just follow up on the previous caller's question. It is not recommended obviously that you try to culture virus if you're only BSL level 2. Probably only those labs that are really expert in this and are a BSL level 3 and above should be even contemplating this. So that's the level BSL three that if you're dealing with a cultured live virus. Okay ready for the next question.

Coordinator: Thank you sir. Next question comes from (Donna Ferguson) your line is open.

(Donna Ferguson): Hi I have some questions about false negative due to inhibitory substances. And our physicians are concerned because some of these patients are receiving breathing treatments. And they want to know if they take a specimen after a breathing treatment if that could lead to false negative.

(Uwe Scherf): Since these are nucleic acid-based tests that are moving forward, I mean we have a good understanding about the extraction approaches that normally these substances are not enough interfering with the assay. So I mean we need to have a compromise – enough approaches available and can be quickly validated. So that was the step that we took in order to allow a faster kind of access to the testing here in our laboratories.

Timothy Stenzel: And to add to that you certainly can take non-reactive samples that are samples in that way and spike in and see if that affects your LOD in any way.

(Donna Ferguson): Thank you.

Coordinator: Thank you. Next question comes from Dr. (Michael Milhoff) your line is open.

Dr. (Michael Milhoff): Hi. My question is in regards to who is eligible to purchase the kits from IDT? Can only governmental labs purchase these kits or can any lab or entity purchase directly from IDT?

Timothy Stenzel: We would – it's not just public health labs that can purchase this. In fact it's probably – but it is let me say that it is any lab qualified to do this testing can certainly order this test from IDT.

Dr. (Michael Milhoff): And the qualification is just a high-complexity lab correct?

Timothy Stenzel: High complexity CLIA certified lab yes.

Dr. (Michael Milhoff): Correct, thank you.

Coordinator: Thank you. Next question comes from (Richard Montegna) your line is open.

(Richard Montegna): Yes thank you for taking the second question. It has to deal with the 30 contrived samples. If we wanted to look at these oral swabs – oropharyngeal swabs and sputum is that 30 of each of those or total of 30?

(Uwe Scherf): Yes, in this case it would be for one of the most challenging matrixes. So if you go for sputum I mean that would be the one that you'd go for.

(Richard Montegna): Okay, thank you very much.

Timothy Stenzel: I want to update my response to the last caller. There may be traditional manufacturers who would also like to get a EUA authorized kit through any of the manufacturers who have an EUA authorization such as IDT who has it under the CDC. You know we understand that having such a kit may be helpful in your test allotment process. And I don't want to exclude those entities from being able to purchase the kit. Okay ready for the next question.

Coordinator: Thank you sir. Next question comes from (William Glover) your line is open.

(William Glover): Hi. Thank you for the question. I just want a clarification answer regarding for high complexity CLIA laboratories that are using the IDT CDC kit. So it was my understanding under the guidance that those laboratories would have to send the first five positive and the first five negatives to another laboratory to get those results confirmed. Is that still the case? If not public health

laboratories that are using the CDC EUA have to send their results to CDC to get confirmed and are presumptive?

Timothy Stenzel: Yes. I understand for public health labs that that is the process. This new guidance has to do when you're developing your own tests in a laboratory developed test, if you were using one that's already authorized by the FDA in this case IDT has authorization under the CDC EUA, this guidance does not apply to you. That test has already been developed. It's already been qualified per lot. And again all that you need to do if you get one of those qualified lots from IDT or any of the follow on manufacturers have an EUA, you simply receive that kit or those kit lots in your lab and follow your normal laboratory procedures when you receive a new kit before you begin testing. There is no notification of the FDA that is required.

But if you were on the call when I mentioned that the public health labs would like to hear, we encourage you to let them know even before you receive an order for a specimen that you have contact with them to let them know that you're going to be initiating testing so they can prepare for dealing with potential positives that you would have.

(Uwe Scherf): I think just to add that the presumptive positives that are then identified after you did your validation and your normal testing, it's clear that they still need to do – need to be sent to the public health labs for confirmation or to the CDC. So I think that's – so to be clear that this is the case.

(William Glover): Thank you.

Timothy Stenzel: I think the best thing is we encourage you to reach out to your local or state public health lab to get further guidance on that.

(William Glover): Thank you.

Coordinator: Thank you. Next question comes from (Tom Griss) your line is open.

(Tom Griss): Hi. I just want to clarify when looking at the LOD – one to two fold LOD is that speaking in log as in tenfold, a hundred fold above or do you literally mean from 1,000 to 2,000 copies that sort of relationship?

(Uwe Scherf): It's from 1 to 2,000. It's close to really the appropriate evaluation there. So if what you're describing is correct it's not necessarily...

((Crosstalk))

(Uwe Scherf): ...yes.

Timothy Stenzel: Yes not (unintelligible) mix. So if your LOD is 1,000 those 20 samples near LOD would have to be in the range of 1,000 to 2,000.

(Tom Griss): Right and then spike in for the positives would be intended to also be around that level for...

(Uwe Scherf): That's correct, yes.

(Tom Griss): And does that imply then you can use the LOD as part of your spike in?

Timothy Stenzel: Can you rephrase the question please?

(Tom Griss): If you get 19 or 20 of 20 is that 20 of the 30 spike in that you need to do then you need 10 additional?

(Uwe Scherf): No, I think the concept would be that remember we described that for the LOD study you can actually use a combined matrix, you know, combined samples that are pooled samples. For the clinical study it's important to have individual samples evaluated because it will give you then the appropriate evaluation tools – the differences in samples. And really what you're doing is you are spiking material into these individual samples to really mimic the appropriate clinical evaluation.

Timothy Stenzel: So to rephrase when you're doing your LOD studies your initial dilution and your final verification of what your LOD is analytically, you can use pooled or clinical samples and non-responsive test negative samples to pool them and do your spike ins and dilution. But when it comes to clinical evaluation you would spike in viral RNA at the levels that are described. But each of those replicates would be in unique negative clinical samples.

(Tom Griss): That makes sense, thank you.

Coordinator: Thank you. Next question comes from (John Baines) your line is open.

(John Baines): Hi yes I believe that you answered it earlier. But if you're getting the IDT kit that have the CDC EUA guidance, the LOD studies and the cross reactivity those are not steps that you need to take in order to begin clinical testing correct?

Timothy Stenzel: That's correct. When you have an EUA authorized test then this new policy is not for you. And, you know, obviously the availability of such kits certainly would make it much easier for labs to get up and going because they don't have to develop the tests themselves. So we encourage that if that's possible for you.

(John Baines): Perfect, thank you.

Coordinator: Thank you. Next question comes from (Laurel Glaser) your line is open.

(Laural Glaser): I'm calling from a CLIA lab. I just have a question. If we're using a manufacturer's kit where we don't know the precise sequences of the primers and probes, can we use in silico LFS if we're going to use it as an LDT?

Timothy Stenzel: So if you're developing a product, you know, I think that's a great question to take offline and send us the question to our email address because we want to get a little bit more specifics but (Uwe Scherf) you can add anything.

(Uwe Scherf): Yes, I mean the point there would be we need to have the sequence information. If the manufacturer is not willing to give it to you, I mean the opportunity from the FDA perspective to contact that manufacturer and get into kind of master file submitted so we have an opportunity to assess it. Because again the concept that we are describing here is nucleic acid base you have to have certain kind of blasts for them so evaluations done. And from our side that means that we accomplish that.

Timothy Stenzel: And we encourage those manufacturers to come in for EUA authorization.

Coordinator: Thank you. Next question comes from (Sopheny Gene) your line is open.

(Sopheny Gene): I believe my questions have already been answered. But I'll rephrase and ask you to confirm. If you are a high complexity, CLIA certified lab using the CDC kit with approved lot numbers you are not required to submit an EUA or to submit notification to the FDA, you can begin clinical testing following verification. My understanding from what you said is that there are no published guidelines but we would use CLIA guidelines on verification.

My second question is if you are validating specimens that are not currently claimed on the CDC kit, i.e., stool, that would require an EUA notification, et cetera per this policy.

Timothy Stenzel: Let me address the stool question first. Yes if you're going to use a sample type that has not been covered under the existing or existing EUAs, we suggest that you send an email to us to discuss how you can make a modification to that. If you're using already an EUA authorized kit, I think the validation required for that will be obviously much more straightforward because much of the work has been done to validate that kit. But we would like to make sure that a novel matrix that hasn't been authorized is going to function adequately and your extraction procedures are good. I will turn this over to (Uwe Scherf) to finish anything on the question. Anything else?

(Uwe Scherf): No, I think you captured.

Timothy Stenzel: Okay. On the first question having to do with what do you need to do if you have an EUA authorized kit. Yes all you need to do is do your normal verification when you receive that kit. You do not need to file an EUA submission or notification with us.

And the second part of that question had to do with guidelines. Could you rephrase that question?

(Sopheny Gene): Oh I was just confirming that we can use standard CLIA guidelines for verification.

Timothy Stenzel: Yes.

(Sopheny Gene): Great, thank you.

Coordinator: That was our last question. I would now like to turn the call back over to Miss Irene Aihie.

Irene Aihie: Thank you. This is Irene Aihie. We appreciate your participation and thoughtful questions. Today's presentation and transcript will remain available on the CDRH Webpage at www.fda.gov/training/cdrhlearn by Friday, March 13. If you have additional questions about today's presentation please use the contact information provided at the end of the slide presentation. As always we appreciate your feedback. Following the conclusion of today's webinar please complete a short 13-question survey about your FDA CDRH webinar experience. The survey can be found at www.fda.gov/cdrhwebinar immediately following the conclusion of today's live webinar.

Again thank you for participating. This concludes today's webinar.

Coordinator: This concludes today's conference. You may disconnect at this time and thank you for joining.

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