

# Clinical Laboratory COVID-19 Response Call

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## Panelists

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**Stuart Streck**, U.S. Department of Transportation (DoT)

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**JASMINE CHAITRAM:** OK, awesome. All right, just give me one more second. Hey, everyone. It was a crazy day. So welcome. Thanks for joining us. So sorry that we're late today. I think Triona might have told you that we had some internet connection problems at CDC, and we had to change location quickly.

So now we're back in my basement. And anyway, I'm glad that we're able to join you and start this call. So thank you to those of you that were patiently waiting to join the Clinical Laboratory COVID-19 Response call. It's hosted by the Division of Laboratory Systems at CDC.

The Division of Laboratory Systems, as I've mentioned before, has a focus on safety and quality, biorepository and data science, informatics, training and workforce development, and also preparedness and emergency response. In particular, we work closely with the clinical labs and public health laboratories to help keep them connected to the responses going on right now for COVID-19 and with the CDC Emergency Operations Center.

So we have some speakers today from CDC. I'm showing the agenda. We may have to move them around until they are able to actually connect and start with some of our other speakers. But before we go into our speakers, I do want to mention a couple of things, as I usually do during these calls.

So the first thing is that our calls are now every two weeks. And so our next call will be on Monday, August 3rd from 3:00 to 4:00 PM. We have links that we provide each week with these slides, and the slides are posted on [cdc.gov/safelabs](https://www.cdc.gov/safelabs), under Tools and Resources. So you can always go there for any information that you missed during the presentation, or just to go back to any important links, or to even hear the transcripts from these calls.

Next is opportunity to give us your feedback on training and workforce development needs. This is the email address where you can send that information. We have asked for feedback in the form of surveys, but we're only going to do those once a month going forward. So for

today's call we're just looking for any feedback that you might have on training and workforce development needs and send that to the email on this slide.

And the next up is our way to ask questions. And so if you use the Q&A button in the Zoom feature, you can submit a question, and we will do our best to answer those questions throughout the call, and if not during the call, then after the call we will have our speakers respond, or we will send-- DLS will send responses as we can. We do get a lot of questions that sometimes are difficult for us to answer or that we use to give us ideas for agenda items for the future. So if your question is not answered during this call, you can always send it to [DLInquiries@cdc.gov](mailto:DLInquiries@cdc.gov) and we will try to answer it there.

And if you are the media, please send your questions to [media@cdc.gov](mailto:media@cdc.gov). And if you're a patient, please direct your questions to your health care provider. And with that, I think we're going to start with our first speaker. And it looks like we were able to get the connection with our CDC folks. And so Rose Martines is going to be our first speaker. And she's going to be talking about infectious disease pathology, specifically autopsies, and public health importance for COVID-19. Rose?

**ROSE MARTINES:** Hi, Jasmine. Sorry, can you hear me?

**JASMINE CHAITRAM:** Yes, I can. Thank you.

**ROSE MARTINES:** Let's start because of the time. So thank you for inviting us to be speaking today. So today I'm going to be talking, as you said-- can you move the next slide, please? Or I can do just-- hello? Thank you. So today I'm going to be talking about the importance of the autopsy surveillance for the public health system. And perhaps you know about autopsy and pathological finds of COVID-19. Our recommendations and COVID-19 guideline are going to be covered by Dr. Sarah Reagan-Steiner from IDPB ([Infectious Diseases Pathology Branch](#)).

So next slide. This is a publication from 2003 where we see that a robust public health system is the best defense against any microbial threat. So we know a long time that it's important to have a public health system working -coordinating a surveillance. Next slide.

I think you moved it back. Sorry. Here I can show the importance of the infectious disease pathology in the public health. It's important to highlight that pathologists are among first there to encounter infectious disease outbreaks in excellent position to discover emerging infectious disease. Our work is a collaborative work with researchers, with epidemiologists, clinicians, veterinarians, and microbiologists. And many examples of recent emerging infectious disease have been diagnosed through autopsies, which are increasingly being viewed as an effective surveillance tool. Next slide.

Autopsy surveillance, it's important to identify clinical and suspected disease process, correlating promoting clinical diagnosis with postmortem findings, elucidate the pathogens of new diseases, and the pathologists should approach the autopsy with a well-constructed

differential diagnosis that provides the framework for appropriated selection of diagnostic specimens and tests. It's important to highlight that more and more we are discovering that animals increasingly are being recognized as a potential factor for infectious disease in affecting humans. So the collaboration with veterinarian pathologists and human pathologists it's a key point for our outbreak investigations.

On the left of the slide we see some examples of CDC collaboration during all these years with some of important respiratory diseases in the world. What we can see on the left is the SARS-CoV infection, identification by IHC on MERS-CoV infection, also by CDC, the hantavirus outbreaks that we had in several countries and the United States, and H1N1. So next slide, please.

Today we are already talking every time in every single moment about COVID-19. And I don't think until now we can say that we have confirmation that the patients are dying with or because of COVID-19. We have so many questions to elucidate in this field. And that the only instrument in medicine now to answer to this crucial question, I think, is the autopsy.

So autopsy case reports in case series have provided useful information regarding the pathogens of COVID-19. Every day we have new publications in showing the importance of the autopsy. Here we see some examples of samples we evaluated at CDC where we see the respiratory system where the SARS-CoV infected epithelium of the upper airway and lower airways are showing the infection of SARS-CoV. And the important find is that you see the alveolar damage is the same thing we are finding in every single publication in the literature involving the lungs.

Our identification in IDPB is showing that SARS-CoV-2 can be detected by immunohistochemistry, electron microscopy, and in different tissues of the lung in the lymph nodes. But it's important to highlight that we are not identifying all the extra pulmonary tissues. In IDPB we use different techniques between IHC, in situ hybridization, several molecular techniques to try to identify and explain the pathogenesis of the SARS-CoV-2.

It's important we remember that in the literature several articles are trying to show also the association of the SARS-CoV-2 with different organs and systems. An example is the possible association of a myocardial injury with COVID-19. Although some COVID-19 cases reported have described findings consistent with a diagnosis of clinically suspect myocarditis, viral myocarditis, SARS-CoV-2 has not been definitively confirmed by myocardial histologic finds in vital genome analysis.

Another example of a research investigation is the histopathologic and viral -] identification of SARS-CoV-2 [in infected patients with gastroenteritis and possible fecal-oral transmission. So one evidence it's showing that is the ACE-2 staining cells in all GI tract, however, no definitive evidence of SARS-CoV-2 was observed in the tissues. Similar studies we are seeing now in brain, kidney, and in different tissues to try to identify SARS-CoV-2. Next slide.

I want to highlight in this slide is the importance of several techniques, old techniques, traditional techniques, and modern techniques are used to try to identify COVID-19 in different organs and tissues. Here is an example of the electron microscopy. What I want to highlight in this is that electron microscopy is a traditional technique, however, the identification of a virus is not always straightforward. Consideration should be given to the mechanism of virus production, including the location inside the cells as well as the appearance of the virus, and if it's showing nuclear capsids and surface spikes.

I think we need to be careful when we analyze the EM samples, because many times we are seeing mistakes of normal cells, or the normal organelles for viral particles. Here it shows some examples of SARS-CoV-2 virus extra cellular in the macrophages where we can see here the characteristic of the virus, if they spikes, and the nucleocapsid. Next slide.

Another example here. Now it's inside type two normocyte where we can see in the arrowhead, we can see surfactants, ending the arrows, we can see the viral inclusions inside membranes where we can see here the specific characteristic of the Coronavirus with these little black dots in the cytoplasm. It's important why I selected the EM for we talk today. It's because now we have-- we are seeing several occasions showing misidentification of Coronavirus particles by EM and are instead showing normal cell structures.

Several articles we are reviewing. And in the meantime, Cynthia Goldsmith] and Hannah Bullock, from our EM team, are intensely working, doing consultations from different countries and from the United States with EM images trying to identify the virus. And in many times we have only normal cells and no viral particles. And, unfortunately, sometimes these images are already published giving some misinterpretation and misinformation to the public health. Next slide.

To finish my part, I think it's important say that autopsy it's important, too, for our investigation with the coronavirus. And, of course, we know that infectious agents can be transmitted during autopsy procedures in an autopsy room. And these are going to be associated with the agent,-- the route of the transmission, --and many time, when we have autopsy room personnel with some disease that are going to be turning this person susceptible to the infectious agent. However, today, with the adequate PPE and training, pathologists are reducing the risk of contamination. In particular, with COVID-19, little is the risk of transmission of the virus infection through autopsy personnel when we are using the PPE.

And the information-- it's a National information-- is showing that we have a low risk, but also our work with the international collaboration with different pathologists and partners, they are showing the same findings. We have little risk associated with the COVID-19 when the pathologist is using appropriate PPE. Next slide for Sarah.

**SARAH REAGAN-STEINER:** Hi. Thank you, Rose. Thanks everybody for the opportunity to present today. So as Rose had mentioned, the valuation for SARS-CoV-2 on post-mortem specimens can be important. This is important for a suspected COVID-19 cases for which testing

was not possible during life or was negative, but COVID-19 is still a concern. So as a result, since February, [guidance for collection and submission of post-mortem specimens from deceased persons with known or suspected COVID-19](#) has been available on the CDC website.

We work to keep this up to date as more has been learned about COVID-19 and as additional resources have been developed. Most recently, this was updated on June 15th to include specific criteria for submission of autopsy tissues to CDC's Infectious Diseases Pathology Branch. This guidance includes information on recommended post-mortem autopsy tissue and swab specimens to collect, biosafety and infection control practices, procedures for submission of post-mortem fixed tissue specimens to CDC, cleaning and waste disposal, transportation of human remains, and links to other resources regarding the post-mortem setting. Next slide.

And I thought I'd focus in on CDC's guidance for post-mortem specimen collection for suspected COVID-19 cases. If an autopsy is performed, collection of a nasopharyngeal, or NP swab, and if possible lung swabs for COVID testing are recommended, as well as separate swab specimens for testing of other respiratory pathogens and other post-mortem testing is indicated, formalin-fixed autopsy tissues from lung and upper airway, and we recommend multiple sections as viral antigens and nucleic acids can be focally distributed in respiratory tissues of patients with COVID-19, and the distribution and quantity can vary among individual patients. So CDC's Infectious Disease Pathology Branch can perform molecular and immunohistochemical testing for SARS-CoV-2 on fixed autopsy tissues from cases that meet specified criteria on our guidance website.

The collection of fixed tissues can be particularly important when respiratory swab-based testing methods aren't available or have been inconclusive. And as with all specimen submissions to CDC, we request that you coordinate through your state health department. And for questions, please contact [IDPBpathology@cdc.gov](mailto:IDPBpathology@cdc.gov). And while not shown here, there may be situations where an autopsy is not performed for a deceased suspected COVID-19 case.

In those settings, a collection of a post-mortem NP swab specimen for COVID-19 testing as well as for testing of other respiratory pathogens is indicated, and health care professionals should work to coordinate post-mortem swab testing with public health and clinical laboratories. So thank you again for your time. And we'd welcome questions.

**JASMINE CHAITRAM:** Thank you both for that great presentation. Just want to tell everybody since we got off to a rocky start, and I didn't really do proper introductions. That was Rose Martines and Sarah Reagan-Steiner, both from the CDC Division of High-Consequence Pathogens and Pathology. And we did get one question. I'm not sure, Rose, if you want to take this question. The question is, if EM is prone to misinterpretation, what testing, visualization, algorithm, combination of tests do you recommend?

**ROSE MARTINES:** Thank you, Elizabeth, for the question. So here in IDPB, what do we use? Of course, after our histopathologic evaluation, we start with the IHCs and we do immunohistochemistry using nucleocapsid IHC staining for detecting the coronavirus antigen

staining in the lungs, in airways. And in this moment, when we have the lesion, is the areas that we select for EM. I think this is important for we correlate into what we are seeing the IHCs.

And another, too, is the in situ hybridization also. So we can combine IHCs and however, we are seeing already here that we have a very good response when we analyze the tissue between in situ and IHC, we have a very good correlation with tissues. So for we avoid this misinterpretation that when we don't see any lesion and we try to do EM without identification of an antigenic reaction, we do a combination. What we do, we select the area in the tissue where we saw the staining, and this area is the area where we're going to move and analyze in the EM for we find the virus.

**JASMINE CHAITRAM:** Thank you. And we have one other question. What is the turnaround time for fixed tissue that's sent to CDC for testing?

**SARAH REAGAN-STEINER:** Hi, this is Sarah Reagan-Steiner. Thanks for the question. So the turnaround time, standardly, for autopsy tissues that are submitted to CDC is six to eight weeks. However, we do recognize that cases submitted for COVID-19 are of particular importance and we work to finalize those as quickly as possible. We do test the autopsy tissues that are submitted via multiple techniques as Dr. Martines had described. And we often receive multiple tissue blocks on each case and perform multiple tests there. And so hope that answers your question. Thank you.

**JASMINE CHAITRAM:** Thank you. I've got another question for you. This person would like to know how long fixation would be needed to make COVID tissue specimens non-infectious. How long fixation would be needed to make them non-infectious?

**SARAH REAGAN-STEINER:** Rose, did you want to take that, or do you want me to?

**ROSE MARTINES:** Yes. I didn't know I was mute. So usually when we detect an infectious disease, doesn't matter if it's COVID-19 or other infection, we recommend between 48 to 72 hours in formalin. And after we have the 72 hours fixed in formalin, we can move it to alcohol, but before we don't recommend. Of course, if you have a small fragment, a tiny piece of fragment, you can reduce the hours, but in the normal autopsy samples, we recommend 72 hours.

**JASMINE CHAITRAM:** And here's another one, would you accept fixed-BAL cell pellet?

**ROSE MARTINES:** Sarah, can I answer?

**SARAH REAGAN-STEINER:** Yes, go ahead.

**ROSE MARTINES:** So usually we don't accept a BAL as a technique for us. Of course, we start to do and when we look at the initial cases as we started to look in some BALs, but usually we recommend that we receive the tissue samples, because in COVID-19 particularly we already

know that the stainings in the technique it's reduced the sensitivity when we have a small sample and a small fragment, so we need a good amount of the tissue for we have the chance of confirmation of the diagnosis.

**JASMINE CHAITRAM:** And I think this is our last question. Can formalin-fixed paraffin embedded tissue be sent in the mail via standard precautions?

**SARAH REAGAN-STEINER:** Yes, so given formalin-fixed paraffin embedded tissues are non-infectious, they can be-- they don't require any specific biosafety during shipment.

**JASMINE CHAITRAM:** We'll thank you both very much again for this great presentation and for joining us on this call today. Our next speaker is going to be Stuart Streck. He was with us, I think, a couple of months ago. He's with the US Department of Transportation. He's going to be talking about packaging and shipping for COVID-19 samples. Stuart?

**STUART STRECK:** Well, good afternoon. Can you hear me all right?

**JASMINE CHAITRAM:** Yep, I can hear you.

**STUART STRECK:** All right, fantastic. Go ahead with the next slide, please.

**JASMINE CHAITRAM:** Sorry. Hold on.

**STUART STRECK:** [INAUDIBLE]

**JASMINE CHAITRAM:** Stuart, are you still there?

**STUART STRECK:** I'm still here. Next slide. Background slide, please. Recently the US DOT in conjunction with some of our sister agencies, and the FAA, and also with carriers throughout the United States, we engaged in a survey of UN3373 packages that are being transported throughout the transportation system.

That is a photograph of me where I visited three of the world hubs located there in the southern region for three of the world's largest carriers. And as I was conducting these surveys, I was looking for-- I was looking for deficiencies within the hazardous materials regulations. And as you can see in some of these photographs, for people who are well adept to shipping UN3373 there's certain things that we're not seeing, and one of those is rigid outer packages. As you can see in the left hand side, I am pinching clearly a vial of UN3373 along with some of the other packages. Next slide.

Some of the issues that we definitely saw was the use of the rigid outer packages. This is a brief diagram of how a package should be used when using a carrier provided envelope or carrier provided box. Essentially when a COVID sample is being shipped, it needs to be in a vial or a primary receptacle that goes into a specimen package, a specimen bag with appropriate

absorbing material, and then that vial in that specimen bag needs to be placed into a rigid outer packaging. The rigid outer packaging needs to contain the certain markings that UN3373 biological substance [INAUDIBLE], but also a 24-hour telephone number in the name of somebody who is going to be responsible for answering the telephone when things happen in transportation.

So if a carrier, or a courier, becomes disabled along the roadway, a package is found, there is a telephone to somebody who has an idea of what exactly is in this particular package while this package is in transportation. Once these packages are packaged correctly, then only then can it be placed into the carrier over-package. What I was seeing was using the carrier box as a primary outer package or the plastic bags as a primarily outer package.

Essentially what I saw was laboratories, hospitals, home health care facilities, senior care facilities that were taking these plastic bags and shoving them full of vials and shipping them off to a COVID testing laboratory. And we were able to backtrack to the laboratory, but also backtrack to the companies, laboratories, individuals who were actually shipping these not in conformance with hazardous materials regulations. So in essence, you have to, as a shipper of UN3373, which does include COVID-19, you're responsible for providing your own packaging in the form of a primary receptacle and secondary package, which is typically the specimen bag and a rigid outer package.

When you examine a carrier package on all three of the major carriers that are used inside the United States, all three have a statement essentially stating that the package that you're providing is not a primary receptacle or an rigid outer packaging for your COVID-19. It's only a covenant. That's all it is. It's an overpackage to consolidate multiple shipping, or it is there to cover your actual package, and it has the appropriate markings. Go ahead, next page.

As a result of our findings, DOT took measured steps. Of those steps, the first thing that we did was we actually provided a safety notice to everybody who was offering UN3373 samples including COVID-19 into transportation. Safety notices are available online at our website. And it has also been dispersed to all major carriers throughout the United States, so that way they can also further to their customer base as samples are being shipped.

Additionally to that aid, COVID-19 or a Category B diagnostic samples poster was developed. It's an 8 by 11 poster that can be easily printed out and posted in laboratory settings where packages are being prepared. It's a simple three step process ensuring that all issues with the primary receptacle, the secondary packaging, and the rigid outer packaging are addressed to include overpacking-- your overpacking permits.

Prior to this happening, we also put together a Transporting Infectious Substances Safely brochure. This is to replace the smaller brochure that had been around since 1996. So we do have a new brochure that is posted on the website. And lastly, we have a webinar that is going to be held this Wednesday, July 22nd. It is available for all parties to attend. There is a maximum CAP of 250. We still have spots.

And we will be addressing things that we found while doing our survey, but also addressing issues that were brought up into the safety notice, kind of give you the nuts and bolts of how to properly ship UN3373 through biological substances category B. Next slide. In the interim, if there are questions, we have people who can provide you answers. We have a hazardous materials information center, 1-800-467-4922. It's manned 9:00 to 5:00 on the weekdays.

Due to COVID-19 restrictions, they may prompt you to send an email if the phone lines are crazy. But we have people who are monitoring the emails and seeing that information. If for some reason that you are unable to reach them, you can also reach out to your CDC counterparts who in turn can answer questions that we had previously addressed, but we can also get a hold of me. I thank you for your time.

**JASMINE CHAITRAM:** Thank you, Stuart. I do have a couple of questions for you. Can you confirm a 24-hour phone number is now required for Category B packages?

**STUART STRECK:** So when you're looking at 173, 197 there is-- excuse me, 199-- there is a requirement in place in 173, 199, A7 that says, name a telephone number and a person who is either knowledgeable about the material being shipped and has comprehensive emergency response and incident mitigation, information for the material, or has immediate access to a person who possesses such knowledge and information, must be included on a written document, such as an airway bill, or bill of lading, or on the outer packaging. So we say an airway bill or a bill of lading, but the problem is, with a UN33-73, there is no physical document that is being handed off to the carrier. So more than likely that number would have to be provided outside of the package to fulfill that requirement for the regulation.

**JASMINE CHAITRAM:** The next question is, blood samples from COVID positive patients have not been shown to have virus, can these blood samples be shipped as diagnostic specimens instead of Category B?

**STUART STRECK:** We do not classify the hazardous material, that is the viability of any virus is going to be best left up to those who determine that it is or it is not.

**JASMINE CHAITRAM:** Does packaging and shipping training need to be done in person for new trainees, or can it be done virtually online? There is some debate about whether or not you need to functionally put together a shipping container with appropriate label the first time versus retrain every two years.

**STUART STRECK:** So that is going to be up to the individual organization who's providing that hazardous material's training. We stipulate that hazardous materials training must be conducted every three years. We do not stipulate whether it has to be in person, online, virtual. We don't even have a minimum test for it. We just say that the individual must be trained and tested, and there must be a record of the training and the testing for available inspectors. However, when we caveat, that strictly for UN3373 Category B biological substances training is, and in one sentence, and I will read it, training, each person who offers or transports a Category

B infectious substance under the provisions of this section must know about the requirements of this section.

So there is a misconception out there that for Category Bs there has to be a training session that's done every three years and it must meet all four training areas of the 49 CFR. With Category B there has to be clear instructions on how to transport and how to package the material, and that individual must have knowledge of that end of this particular section, not the entire book. So most health departments and most laboratories who ship both Category A and Category B will cover Category B because of the Category A training. They can strictly ship in Category B where the minimum training requirement is just a knowledge of and a verification of that knowledge, would be how you actually ship it and how it's [INAUDIBLE]. So I just put that out there.

**JASMINE CHAITRAM:** Great. Can you real quick just mention how folks can register for the webinar that you said was going to happen on July 22nd?

**STUART STRECK:** So on our website we do have a training link. And I was fortunate enough-- CDC also put it out through their different communication systems as well. If you're unable to find that, please-- on the CDC site-- let me know, and I will make sure that you get that information. I will forward that to you, and you're welcome to send them over to all the members who work [INAUDIBLE].

**JASMINE CHAITRAM:** Thank you very much, Stuart, for joining us today. And for folks that still need help with registering for the webinar, you can also send an email to [DLInquiries@CDC.gov](mailto:DLInquiries@CDC.gov), and we can get the information to you. Our next update is from the US Food and Drug Administration. Dr. Tim Stenzel who's been on these calls before, will be giving that update.

**TIM STENZEL:** Hey, Jasmine. I just want to do a sound check. Can you hear me OK?

**JASMINE CHAITRAM:** Yeah, you sound great.

**TIM STENZEL:** Great. First question is, are there any plans to relax the requirements for collecting samples from places of employment or schools, specifically relaxing the requirement for on-site supervised collection and/or the requirement to have a prescription? I understand the virtual observed collections are considered the same as home testing and will require a separate EUA, even if these were performed in a more structured environment, such as a place of business. We have and continue to authorize and grant EUAs based on supportive information for collection on unsupervised samples. And we look forward to doing that.

We have seen data from some where unsupervised samples do not yield accurate information. So doing the appropriate validation is very important. And we're very willing, and this is a high priority for our office when these requests come in for this type of work. Second question is, is there any data available for antigen testing? Yes, we post all of the authorized tests, including

the antigen test and their performance information, on the FDA website. By clicking on-- in this case, their instructions for use through IFU, you can view the performance testing.

And for those that are familiar with the bar for antigen testing is that we expect that relative to a high sensitivity molecular assay that antigen testing perform at least 80% sensitivity relative to the molecular test. We've just updated emergency use authorizations with direct swabs, so I encourage you to check out their new performance information in their IFU. Next question is, most companies report some cross-reactivity with other antibodies, this is referring to serology tests when serum from patients with other infections or autoimmune disease are tested, therefore, specificity does not seem to be as high as the estimates that you quote. So one thing to note is that, yes, we do require cross-reactivity testing for serology developers. And if there is any cross-reactivity that is further investigated and considered part of the authorization, and all that cross-reactivity information is presented in these IFUs or EUA summaries.

Now, oftentimes, these cross-reacting samples are presented in this information not in a population-based study where you know the percentages of those potentially cross-reacting samples might be seen in your population. So it doesn't-- you do need to take a look at the population that you test and find out what might affect this. So one of the things that we have been paying attention to is HIV cross-reactivity. And there were some reports for the previous SARS where there could be some, so we do pay close attention to that.

So please do check the instructions for use, and check this cross-reactivity testing and the information. But also we do require a minimum number of unselected negative samples, so you can see the overall performance in those populations. And some of the developers have done thousands of samples. And so I think they do have really good performance estimates regarding specificity.

And then with serology tests, even with a great serology test, you can have false positives. So laboratorians and clinicians should always consider getting a second different serology test if that's important. Next question is, with little such testing required for EUA authorization, are we supposed to believe the reported sensitivity and specificity for these tests?

This question and the person who poses it points out an important fact, the bar for EUA authorization is significantly lower than for a regular submission. This is due to the emergent nature of the pandemic and the need to get testing out there as soon as possible. We do require the listing of the 95% confidence intervals around all of the data regarding sensitivity and specificity.

So that's important statistical information to tell you that even though they measured the sensitivity or specificity to be the  $x$  and  $y$ , that the statistics tells you that actual performance could be anywhere within potentially that 95% confidence interval window. So it's an additional statistical aid to inform decision-making about tests. And, of course, in the beginning, we allowed contrived samples, because actual patient samples were very limited. As the pandemic

grew, actual patient samples became available, and we began requiring testing on actual patient samples to help further address this question.

And as always, clinical judgment should be used to make sure that the test results make sense given the patient's symptoms and/or their history. Next question, can folks share how they are reporting pooled results and who is performing pooled results? So over the weekend we authorized the first pooled EUA test, that's Quest. We will be posting all these authorizations once we make this decision. Of course, any lab that wants to pool can validate, can notify us, and begin testing and submit the pooled validation data within 15 business days for the FDA to review and consider for authorization.

We do have some information, and it may grow, but as far as a negative result goes from a negative pool, you can from the negative pool report out individuals as negative. If a pool is positive or indeterminate, all the samples in that pool should be tested individually, and only those individual results reported to patients. Hopefully that helps. Is pooling acceptable for diagnosis of suspected COVID-19 cases? Short answer is yes.

Where would I find a list of companies that sell neutralization antibody tests? So we are reviewing these tests. And we will post the authorizations on the FDA website when that occurs. And developers of neutralization assays can validate their tests, notify the FDA. Submit their data within 15 business days, and the FDA can list these assays following that. Many companies-- next question-- are developing triplexes, or multi-analyte or multi-virus panels-- that's true-- what is the value, added value, of this kind of test? Well, symptoms can-- these are respiratory viruses, and symptoms can overlap. And the FDA considers multiplex devices to be a potential valuable way to increase testing for respiratory pathogens while preserving reagents.

So instead of having to do, say, a SARS testing, a flu test, they can be combined into one from one respiratory sample. Next question is, has the CDC, FDA, CMS created a target limit for detection from manufacturers of multi-analytic respiratory panels. No, we haven't. We expect that the clinical performance, sensitivity PPA, and specificity NPA are sufficient to support authorization. We also do require LOD studies, and those are reported in the UA summaries, or IFUs.

Next question, if the manufacturer of the COVID test has been approved for EUA for their instruments, do we need to obtain another EUA for the COVID test in our own lab? So if the instrument is not in the EUA authorized test package insert, then you can validate another instrument in your lab, and simply validate it, make sure that it is validated, you are not required to get an EUA authorization, and you're not required to notify us. But you can reach out to us through our FDA template inbox for further discussion as needed.

The final question is, are there any plans to include the ABI QuantStudio DX in the CDC's EUA? So first of all, check out the FDA's FAQ website, the ABI QuantStudio quantitative DX is listed on the list of alternate instruments. This means that you can, for the CDC assay, if you get those

reagents, say, from another supplier, you can validate this instrument as an alternate, and you're not required to submit an EUA for that change.

And then as far as the CDC adding it to their EUA, they're just like any other developer, they're a special developer, of course, and they determine what instruments go into their own EUA authorization. And we're always ready and willing to work with any developer including CDC to update their EUA authorizations. And so with that, thanks, and that ends my discussion.

**JASMINE CHAITRAM:** Thank you both so much, Tim, for answering all those questions. We got a few more this week, but in the interest of time, I'm going to move to our next speaker and last topic, which has been of a lot of interest to a lot of people. I think, in the last couple weeks we've gotten a lot of questions. So here to give us an update is Sara Brenner. She's from the FDA, but sitting in a new role right now at HHS, and maybe she'll mention that. And she will talk about laboratory reporting requirements. Sara?

**SARA BRENNER:** Thank you, Jasmine. You can hear me, yes?

**JASMINE CHAITRAM:** Yes.

**SARA BRENNER:** Fantastic. And I'll just ask you to advance the slides. There aren't very many. So go ahead to the next one. As Jasmine mentioned, we have been getting a lot of questions about laboratory reporting. When I say we, I mean, the interagencies, including CDC, some to FDA, and, of course, directly to HHS. So most of the questions over the last week, we'll say, have to do with clinical labs and hospitals and some confusion around reporting there.

I'm not going to speak about that. Today we're working on some clarifications that will hopefully be updated to the July 10 language very soon. The takeaway message there is we want as much data reported with as little burden as possible. So the goal is to streamline data reporting and to ensure that the data that's received centrally at HHS is accessible to all of the interagencies, meaning CDC and other agencies that need that data. So hopefully we'll have some clarifications for you all soon on that.

But the focus of these few slides here today has more to do with the June 4th guidance that came out for laboratory reporting for COVID-19 related tests. So if you've already read the June 4 guidance, this will mostly be a review, but we'll go ahead and go for it. And if we have any time, we can take questions, or you can feel free to reach out to me directly afterwards with any questions.

So the June 4 guidance is essentially superseding all previous guidance and applies to all laboratories, or all locations, that perform clinical diagnostic testing under CLIA. So there's been a little bit of confusion about how laboratories are defined, but essentially any location that is performing a clinical diagnostic test for COVID, any of the three categories of tests, will be subject to the June 4 reporting guidance. So there are facilities and other locations that are

offering point of care or even in-home testing. So if you're operating under CLIA, you are subject to those reporting guidelines. Next slide.

Fantastic. Outlined in the details of the actual document, there are basically three primary ways that you can submit COVID-19 test result data directly to the state or local health department, public health department, through a centralized platform such as AIMS through the state or regional health information exchange. Those are the primary routes. Next slide.

Now, this is where things get interesting. So as everyone has read it, has taken note, there are quite a few categories of data elements that are to be recorded. Some of those are not traditionally captured by laboratories, but are captured in the clinical setting, including some ask on order entry questions. So we've been working very busily to help define and provide technical specifications as well as coding parameters and value sets for each one of these data elements.

So I'm not going to go into all of the details today on this call, but hopefully in a future call, as soon as our further technical specifications document is cleared and released to the public, which will hopefully happen very soon, we're hoping this week, we'll be able to do a deeper dive on the technical specifications for each of these data elements. The goal is to standardize them, so that when they come in, the data, through reporting, the data is harmonized every step of the way. This will help states, this will help the federal government broadly, and generally it will help facilitate the collection of more comprehensive and high-quality data that we can then perform any number of analytics on for any number of purposes. But I'll just leave it there for now. And go to the next slide, please.

So I wanted to focus just a little bit on this particular section. It's the last several questions, I think, that are outlined. They're asked on order of entry, and those will be obtained by the ordering provider of the test. And so we've worked with HHS and the interagencies to help flesh out what these questions really are intended to ask. In the guidance, they're very brief. They're not even full sentences or full questions. So what we did was we fleshed out essentially a script that clinicians could use, or ordering providers could use, to obtain the actual data or the response that we are looking for.

So those have just been posted. A little bit more of an expanded version from what you see here on this slide has been posted on CDC's website. And it will be updated again, I think, at some point today. And the update that will happen today, or very soon, will sort of replace the third column with even more technical detail around what the value sets and data input would be for each one of these, each one of these elements. And by that I mean we actually detail out the LOINC codes, HL7 messaging, the value sets from which you can choose, the SNOMED CT values that would be used, and so on and so forth, including the formats that should be used.

So all of this is meant to take the guesswork on how to answer-- how to ask and how to answer these, and, again, to improve the quality and standardization and the harmonizing efforts that we're doing on the back end as the data is coming in at the state and federal levels. So we

thank you very much for your patience as we continue to flesh out the additional data elements and technical details around these questions and around all of the other data elements. We're certainly engaged with the community and doing our very best to try to make this as easy, or as least difficult, for the stakeholder community to implement. And hopefully when everything is in place, reporting will really be streamlined and really be incredibly high quality for COVID-related diagnostics and tests.

Next slide, please. I think that's it, actually. And the last slide just has a few links on it. Yeah, so the actual June 4th guidance is the first link, FAQs from HHS is the second link, and CDC's lab reporting website, which has the AOE questions that were on the previous slide, and a great deal of additional resources around that last link. So, again, I think we're out of time today. But if you do have any questions, if you would like to provide input, or if you just want to make sure that your input that you've already provided is being looked at and considered, please feel free to reach out to me directly. Thank you very much.

**JASMINE CHAITRAM:** Thank you, Sara. And I know we're out of time. We're just a couple minutes over. But we do have Dr. Ren Salerno from the Division of Laboratory Systems that also has some important information related to data reporting. And I think it would be helpful for him to go through those slides quickly because we've had a couple of questions about reporting for testing that's being done for clinical trials. Ren?

**REN SALERNO:** Thanks, Jasmine. I'll be really quick. I won't read these slides. But I do want to point out on that same website that Sarah just referenced, the CDC, so if you go to CDC COVID-- you Google CDC COVID laboratory, you're going to get the [laboratory page](#), and on the laboratory page there's a reporting laboratory data button, hit that button, and you'll see the ask on order entry information on [that page](#), but also there's a series of frequently asked questions at the bottom of [that page](#). And all I wanted to tell everybody was that we have two brand new frequently asked questions on that page about clinical research trial reporting, so reporting for clinical research trials, which is a little bit different than the standard reporting for diagnostic testing.

And so for those who are doing clinical research trials and are really interested in reporting, please refer to those FAQs. I won't read them here, but these slides will be in the report out, or the recording for this-- and on the website-- for this particular meeting, so you can look at the slides if you need to, or you can just go to the website and look at those two new FAQs, which are number seven and eight. Thanks, Jasmine.

**JASMINE CHAITRAM:** Thank you, Ren. And, again, apologies for the late start today and for going over. We do appreciate your time and value it. And we are grateful that you could spend this time with us. We're grateful for all the questions that you submit. So keep on submitting those. We will do our best to answer the ones that were not answered live today.

And as Ren mentioned, the transcript is recorded, and we will have all the slides and all of the speaker notes as well as the audio on our website Safe Labs-- sorry-- [CDC.gov/Safe Labs](https://www.cdc.gov/Safe-Labs), Tools

and Resources. And as always, send any questions you might have to [DLInquiries@CDC.gov](mailto:DLInquiries@CDC.gov).  
And thank you very much for all that you're doing. And we will talk to you in two weeks.