Clinical Laboratory COVID-19 Response Call

June 14, 2021

Agenda:

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- **SARS-CoV-2 Variants Update**
  - Steve Oberste, CDC Laboratory and Testing Task Force for the COVID-19 Response
- **National Wastewater Surveillance System**
  - Amy Kirby, CDC Division of Foodborne, Waterborne, and Environmental Diseases (DFWED)
- **Sodium Citrate Tubes Supply Shortage**
  - Linda Ricci, U.S. Food and Drug Administration (FDA)
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  - Muktha Natrajan, CDC Division of Laboratory Systems (DLS)

JASMINE CHAITRAM: Hi, everyone. I am Jasmine Chaitram. Welcome to the Clinical Laboratory COVID-19 Response Call. I'm Associate Director for Laboratory Preparedness in the Division of Laboratory Systems here at CDC. And our division has been hosting these calls since March of 2020.

It's been a month since we've had our last call, so it feels a little bit off today. But I'm glad you're here with us. We've got a great agenda for you. And before we do that, I just want to tell you a few things about the division and go over a few housekeeping things.

So the Division of Laboratory Systems has been supporting clinical and public health laboratories prior to the pandemic and throughout. There are several topic areas that we focus on including quality and safety, training and workforce development, informatics, biorepository and data science, and preparedness. And we are here hosting these calls to help you through this response.

And hopefully, the topics that we present answer a lot of your questions. If they don't, please let us know. There's lots of ways to provide feedback, and I'm going to tell you about that in just a second. As I said, we've got a full agenda today. So we are going to get started in just a minute.

First of all, I wanted to mention our CDC Preparedness Portal. This is where a lot of our information is archived. So all of the calls, the slides from the calls, transcripts, audio

can be found here as well as any of our LOCS messages. That's the Laboratory Outreach Communication System.
We sent out several LOCS messages today in fact. So hopefully you're receiving them. If not, you can send us an email at LOCS@cdc.gov. And we can help you with getting signed up to be on our distribution list.
Our next call will be on Monday, June 28, so two weeks from now. We had skipped the last call because it fell on a holiday, but we are back to our two-week schedule. And we will start at 3:00 PM on that Monday. We are asking specifically for training and workforce development needs. So please send those to LabTrainingNeeds@cdc.gov.
And I guess we are at the point where we can go over how to ask a question. I've mentioned this before. We really want you to use the Q&A button in the Zoom feature so that we can record your question. And especially if we're not able to answer your question on today's call, it would be helpful for you to include an email address so that we can contact you for follow up.
We do get a lot of questions on the call. We can't get through all of them, unfortunately. So we do try to either answer them by email or in a future call. And so just try to have your email address in there if you want to hear from us.
I understand sometimes you want to do an anonymous submission. That's OK. But just know that if we don't answer your question and we don't have your email, we may not be able to get back to you.
Also, just a reminder with questions, these calls are targeted for clinical and public health laboratories. And the subject matter should be around clinical laboratory testing for COVID-19. So questions beyond that will be difficult for us to answer. We may not have subject-matter experts on the phone. We will try to follow up where we can, but please try to narrow those questions on that particular topic area.
All right, and then just a quick reminder that if we have speakers presenting material, especially those outside of CDC, that the content does not necessarily reflect CDC's official position. And that is the same for any of the slides that we post on our website.
And with that, we are going to go ahead and start with our first topic on our agenda. And this is going to be an update on variants. And Steve Oberste is now on the Laboratory and Testing Task Force.
He has taken over for Vivien Dugan who was on several of these calls. And now Steve has been on a few for us, and we appreciate him being here. And we are going to go ahead with his update. Thank you, Steve.
STEVE OBERSTE: Thanks. Good afternoon, everybody. Next slide, please.

So as expected, multiple variants of SARS-CoV-2 have emerged through the pandemic, both in the US and abroad. The biological properties of these variants may be slightly different from the parental virus from which they're derived. And I think it's all clear by now to most of us.

These can include transmissibility, disease severity, as well as things like potential impact on critical countermeasures that would include vaccines, therapeutics, and diagnostics. The CDC monitors these strains and the different variants through the National SARS-CoV-2 Strain Surveillance System, or NS3. And this is comprised of several different components.

They include sequencing at CDC of specimens that are received from state, local, and territorial public health laboratories, contracts with some large commercial diagnostic laboratories and academic partners. The diagnostic labs receive a number of specimens for clinical diagnostics and then have those that they can sequence. And we also help support some of the state health departments to improve sequencing capacity at the state or local level. Next slide, please. Thanks.

Again, there are a number of variants that have arisen through mutation in the viral genome. These are routinely monitored through our sequence-based surveillance through laboratory studies as well as epidemiological investigations. There's a US government Interagency Group that's comprised of experts from the CDC, from NIH, FDA, from BARDA, and from Department of Defense. And this group has developed a variant classification scheme that defines three different classes of SARS-CoV-2 variants. These are variants of interest, variants of concern, and variant of high consequence. Next slide, please.

Variants of interest have specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape. So for example, these can be in the receptor-binding domain of the spike protein for those that might affect transmission or immune escape. They might be in the nucleocapsid region where a lot of diagnostic targets or diagnostic assays are targeted, for example. And for a variant of interest, there may be evidence of that variant causing an increased proportion of cases or specific outbreak clusters.

So for example, these may be-- so for variant of interest, it's basically there's a genetic marker. So we don't necessarily know that there's a phenotype associated with it. However, it's in a location of the genome where protein that would seem to indicate that there's potential for causing a problem.

A variant of concern, on the other hand, is a slightly elevated level where there's actually evidence of impact on diagnostics, treatments, or vaccines. Therefore, there actually been experimentation done or work with field samples, epidemiology. So in my mind, a variant of interest kind of raises your level of interest somewhat. And it triggers laboratory data, laboratory work of some kind. There might also be evidence of increased transmissibility or evidence of increased disease severity.
Then the highest level of variant is a variant of high consequence. This is something that would have known potentially serious impact on medical countermeasures like evading vaccines or evading treatments. Currently there are no SARS-CoV-2 variants that have risen to the level of high consequence. Next slide, please.
These are the variants of interest and variants of concern that have been named so far. This is from the WHO nomenclature that was just announced a couple of weeks ago. They've identified four variants of concern shown there on the left as well as six variants of interest. And just note that these designations may be somewhat different from country to country and may differ from what WHO has because they're always defined in a particular context.
The other thing to point out is that these names, the new Greek letter designations are not necessarily a complete substitution for the old names, so the Pango lineages shown there on the right, like B.1.1.7. But rather, they're meant to be a simpler form that's more easily pronounceable, easier to remember, especially in communications with the public and with the media. They're also meant to be non-stigmatizing. So we don't call out a particular country where they simply may have been identified, but the country itself is not necessarily responsible for that variant.
As I said, the Pango lineages and other naming conventions will continue to be used in technical communications. And CDC has added these new names to our variant of concern and variant of interest tables with footnotes in some of our other pages just to make it so everyone kind of has all of the different names at hand for easy reference. Next slide, please.
So we estimate the proportion of SARS-CoV-2 variants on a biweekly basis with updates during the week. So sequences from specimens that are collected over a two-week period are then used to estimate the proportions both nationally and regionally for that period. We use weighted proportions that are adjusted to correct for potential non-random sampling of sequencing data over time and across different states. To be a little bit more representative, we asked large states to send more examples, especially for

sequencing. And we try to sample those also at a higher level through some of our other colleagues who are providing partners who are providing sequences.

We also have a separate system or related system, I guess, that's called nowcasting that uses a more complex regression model of weighted sequencing data to estimate proportions and have predicted prediction intervals. So basically, the weighted proportion is using all the data that we have within a given period to estimate the proportions in that period, whereas the nowcast estimates will then-- and that's by definition, something in the past because we've completed all the sequencing or most of the sequencing for that period, whereas the nowcast is meant to predict right to today's date or in the case of whatever the date of the actual nowcast is, which sometimes has some more preliminary data that's for the most recent time period. And so it's a little bit more not necessarily speculative, but it's not quite as precise. And therefore, there are prediction intervals that go with that.

All of these are posted on our COVID Data Tracker (see the “Genomic Surveillance” section) every Tuesday. So there'll be new data coming out tomorrow. Next slide, please.

This shows an example from what we had last put up last week for the weighted estimates. And you can just see by the color coding on the bars on the left, you can just look at the size of the bars and see how B.1.1.7 has come to predominate over time. The P.1 variant has increased. That's that kind of darkest orange color.

The B.1.617.2, which is of interest right now, is that darker purple toward the bottom. It's been increasing steadily. It's at about 2.5% as of last week compared to P.1 at 8.1% and B.1.1.7 at 69.2%.

Most of the lineages have remained relatively steady over time. P.1 increased a little bit. B.1.617.2 had also increased a little bit. The proportions that we showed in the weighted proportions last week were all within the nowcast prediction intervals, helping us have some confidence that those are giving us good numbers. Next slide, please.

This is the regional prevalence. So we also do this for regional as well as nationally. And you can just see by the different pie charts for each of the defined HHS regions that, not surprisingly, there are different proportions of different variants in the different regions. So for example, to B.1.617.2 is at 8% or was at was at 8.8% in region 8, sort of the Northern Rocky Mountain region, a little bit lower than that, 5.7% in region 7, and over 2% in several other regions.

You can see also by the P.1 was higher in region 5 and in region 10. And we can use this to look at changes over time and whether there needs to be changes in

recommendations, for example, for therapeutic monoclonal antibodies. Next slide, please.

This shows the nowcast estimates that go back up through the 5th of June. Again, the next time period will come out in tomorrow's data updates. But you can see, it was predicted that P.1 would be at 11.2% by that 6th of June as opposed to the 22nd of May, which is what we had for the weighted percentages.

B.1.617.2 is predicted to be as high as 6.1% nationally, whereas B117 was predicted to remain right at the same at 69.2%. All of the other variants either were predicted to remain the same or to decrease slightly. Next slide, please.

And here I just want to call out the-- compare the regional nowcast differences for two different time intervals. And if you look on the left-- and I'll point specifically, say, to region 8-- and you see that darkest purple wedge on the left-hand side-- I apologize, the pies are slightly different sizes. But I think you can still tell the differences in the size of the wedge.

And compare that to that same dark purple color in region 8 on the right-hand panel, which is the period two weeks later. And you can see how it's increased considerably, whereas the proportions of P1 were predicted to remain generally stable in most regions with some fluctuations. As I mentioned, that can have some implications for efficacy of certain therapeutic monoclonal antibody products that might be used in different regions, whereas the B.1.617.2 is predicted to increase particularly in regions 6 through 9, so toward the Western part of the country. Next slide, please.

And we also put out a table of variants of concern proportions by state. This shows as of June 8. So again, last week's data. This is actually for a four-week period, not just two weeks. And that's because we need enough sequences from each state to make reasonable predictions.

These are from states that have submitted at least 300 sequences over a given four-week period. So it's never going to be or almost never going to be all 50 states. And so it's usually in the range of about 30 states.

Again, B.1.1.7 predominates nationwide. It's the highest on average nationwide, but it's also quite high in most states. The B.1.351, which is a variant of concern, proportions have remained quite low. It's only above 3%, I think, in Oregon.

The B.1.427/B.1.429, which emerged in the West Coast in California and were at quite high levels early on, have been declining steadily and now are relatively low. It's down in the 9% range in California, whereas it was over 20% just a couple of months ago. And

then P.1 proportion is high, particularly in Illinois and Indiana, as well as Massachusetts and several Western states.

So all of these data are on the CDC COVID Data Tracker. Like I said, they're updated on Tuesday afternoons. So you can take a look there. And there's of course links to the variant definitions and lots of other useful information.

I think that's my last slide. Thank you.

JASMINE CHAITRAM: Thank you so much, Steve. We had a couple of questions that were submitted through our LOCS mailbox right before the call. So I was going to ask you those. The first one is, "With the concern about new variants, has anyone looked at point-of-care testing such as Abbott ID NOW, or BinaxNOW™, or the BD Veritor™ Plus System as to their ability to detect the variants? Does it change the sensitivity in particular?"

STEVE OBERSTE: Yeah, thanks for that question. The manufacturers who have an EUA assay are required to monitor the performance of their tests. FDA and the US Government Interagency Group also monitor performance of assays. In the case of molecular assays, obviously that's pretty easy because we can simply look at the target sequences where they're known. And you can predict whether there are nucleotide changes that have accumulated in those areas and whether that's likely to affect the assay.

Most of the antigen tests are targeting the nucleocapsid region, which has not changed as much, although there are specific changes that have occurred in some lineages. And so that's a little bit harder to predict because the actual target of the antibodies is not always known. But again, the manufacturers and FDA are monitoring those with some wet testing where they have the strains available.

JASMINE CHAITRAM: Great. Thanks. The other question we got was, "Do we have any data on the effectiveness of the current vaccines against the UK and Delta variants?"

STEVE OBERSTE: Yeah. There's some preliminary data. There are a couple of things that are either published or in preprint format that show that sera from people with--vaccinated individuals have somewhat reduced neutralization capacity. However, it's not really high. So it's generally in the three to fourfold range for the Delta variant. That's the B.1.617.2.

Now, we don't know what the minimum titer is, the actual correlative protection, which is an area of active research of course. That's an important question. However, it's generally thought that the vaccines are still effective. And certainly, there's no data to

date that would show that that's not so. So there's nothing to indicate that the expansion of this variant is due to vaccine escape.

JASMINE CHAITRAM: OK, great. And we did get one more question while you were giving your presentation. And the question is, "Is the AY.1 variant still considered Delta because it is B.1.617.2 plus K417N?"

STEVE OBERSTE: Yeah, that's a good question. It's a little bit of a technicality. I think it is still considered under Delta, but I haven't actually checked on the WHO website since AY.1 was first identified.

And that's one of the complications of the way the lineages are assigned, because it's a phylogenetic lineage. And of course, as the viruses continue to evolve, they will continue to change and will continue to diverge from one another. And so in some ways, some of these, we're left with drawing lines that are somewhat arbitrary to separate two different lineages. I think the fact that it's essentially B.1.617.2 plus a little bit probably means it's not that different from B.1.617.2. But I don't know there's been any actual work to show a different phenotype.

JASMINE CHAITRAM: OK. Well, thank you so much, Steve, for being here today. We don't have any other questions for you. So I do appreciate your time.

We will go to our next speaker. And that is going to be Amy Kirby. And she is going to be talking about the National Wastewater Surveillance System, (NWSS).. And she is with the Division of Foodborne, Waterborne, and Environmental Diseases at CDC. So thank you, Amy, for being here.

AMY KIRBY: Great. Thank you. It is my pleasure to be here. I will start up front by acknowledging that I'm going to violate Jasmine's note that this is only clinical.

The National Wastewater Surveillance is very much not clinical testing, but it does complement clinical surveillance. And so I think it's worth giving a little primer about what NWSS, as we call it, is, and how it's set up, and how this data is being used to inform the response. Next slide, please.

So a little overview of why wastewater surveillance is a value for SARS-CoV-2. The first is that we know that about 50% of people will shed SARS-CoV-2 RNA in their stool when they're infected. And this shedding happens in all types of infections. So it happens in people that have symptoms. It happens in asymptomatic cases, and it happens in children and adults. And so we can use wastewater surveillance to get systematic data on the overall burden of infection, unlike clinical surveillance which we know is going to be skewed towards severe and symptomatic cases.

Second, wastewater surveillance is independent of health care seeking behavior. So it doesn't matter if people go to the doctor or if they have access to testing. We can detect those cases in the community through wastewater surveillance. And so that makes it a very powerful data source for understanding what's going on in communities.
Third, wastewater is efficient. We know that one sample coming into a wastewater treatment plant can represent hundreds, thousands, or even millions of people in the largest systems.
And finally, it's fast. So we can have data from wastewater within five to seven days of when that toilet is flushed. And this compares to about two weeks for some of the clinical surveillance systems. So that one-week lead time that we see routinely with wastewater data is really significant for COVID surveillance because you can do a lot in that week to prepare communities for the increase in cases that you know is coming.
Next slide.
So as great as wastewater surveillance is, it is a different approach to surveillance. So we're used to our disease surveillance systems really being focused on those top three layers of the surveillance pyramid that I'm showing here-- deaths, hospitalization, ambulatory care, the things that are linked to clinical care. But wastewater surveillance is not in any of those layers. It is the foundational layer, community infections.
And there is no way to link wastewater surveillance data to a specific case. So you can know that there are cases in the community, but you cannot know who is infected. And so we have to think differently about how this data can be used. And one of the things that we are hearing consistently from our jurisdictions is that wastewater surveillance is really valuable to them as independent confirmation of true increases and decreases in cases.
Across the COVID response, they're looking at 13 different indicators to understand what's going on in their communities. The majority of those, really 12 of them, are linked to clinical care. Wastewater is the only one that's not. And so it responds to different drivers. And often, when those clinical indicators are conflicting, wastewater data can help our jurisdictions understand what's really going on and cut through all of that noise to really find the signal.
Second, wastewater data can help with health equity issues. We've seen our jurisdictions using wastewater data to understand what's going on in communities where clinical testing data is either completely unavailable or limited. And then they're using that information to do things like site mobile testing units and allocate hospital resources.

Finally, we know that some of our jurisdictions are using wastewater surveillance data to do near-term forecasting of cases and hospital utilization, because we know that when you see increases in wastewater, in about a week you're going to be seeing increases in cases and the testing that goes along with that. And about a week after that, some of those cases are going to start showing up at local hospitals for care. So that increased time can allow them again to more effectively distribute resources to communities where they know there's a need coming in the near term.

One thing that some jurisdictions are using it for but that we don't really emphasize is using wastewater surveillance to estimate point prevalence or case counts in the community. Now, there are models that can do this, but they are not very precise. And even worse, the precision varies from jurisdiction to jurisdiction based on how the wastewater systems are designed and operated. So although it can be useful in a single jurisdiction, it really doesn't generate data that's comparable between jurisdictions. And so that's not something that we think is useful at a national scale.

Instead, we really emphasize that the most robust metric from wastewater surveillance is trend characterization. Are cases going up? Are they plateaued? Are they decreasing in a community? Next slide.

So in September of 2020, we established the National Wastewater Surveillance System. And this is a schematic of how data flows within the system. So starting in the top left, communities, of course, are who is generating the waste water. In systems that are sewered, which is about 75% of US communities, the wastewater will flow to a wastewater treatment plant. There, the utility operators will collect a sample of the wastewater and submit it to a laboratory for testing.

The lab will do quantitative testing for SARS-CoV-2 RNA along with other markers for quality control and test efficiency in those samples. And then that data is submitted to the health department, who in turn submits it to the CDC decipher system. And I'll show you more about that in just a minute. That's where we do analysis to provide consistent data analysis and reporting. And those results are then returned back to the health department for action.

CDC will also be doing national summaries and sharing those. And we plan to eventually push this data public to COVID Data Tracker, although that's probably a couple of months off at this point. Next slide.

So participation in NWSS has grown very quickly, which I think is really an indication of how valuable this data is to the jurisdictions that are standing up wastewater surveillance. So the map I'm showing you there is all of the jurisdictions that are using

CDC funds to support wastewater surveillance. The blue states and territories and the red stars are currently funded using COVID funds to support wastewater surveillance. And then the pink ones have pending awards coming through ELC. We currently have a total of 36 jurisdictions that will be using CDC funds to support wastewater surveillance. And then the graph on the right is the number of samples that have been submitted to our decipher system. So the system was opened for data submission at the beginning of January of this year. And just last week, we crossed 10,000 unique wastewater samples in the system. Next slide.

So this is a screenshot of the decipher results dashboard, so how results go back to our state health department partners for action. The primary display is shown there in panel one. So you can see in this example, all of the locations where wastewater samples are being collected on the map. And then those dots are color coded by the current trend category. So is it increasing, plateaued, or decreasing?

If a trend is sustained over five or more data points, we consider it sustained. And so you can see that at this point-- this was back in March-- Ohio was not doing great. All of their utilities were either in a sustained increase in red, or they were plateaued and yellow with that one blue exception. I'm happy to report that Ohio is in much better shape now.

You can also dive into any of those data points in greater detail. And that's shown panel in panel two. So for each sample location, we have a time series graph. The wastewater data shown in black.

We can also import case data from the population that the wastewater is collected from. So wastewater systems, their boundaries don't often overlap with other jurisdictional boundaries like a county or a city. And so we want to be very sure that the cases that we're comparing to wastewater data are actually from that same geographic location. So we have some codes that will allow extraction of that limited data set. And we can present that here shown in the gray bars. Along the x-axis of each of those is a bar chart that shows the trend categorization for that sample location over time.

We also have a couple of quick view displays. So number 3 is our trend classification grid. That just shows the percentage of sampling locations in each trend category for the latest sampling round. And then number 4 is the alerts list. It's empty in this display, but if a value was higher than we would expect based on the most recent data points, an alert would be displayed there.

This is not necessarily an alert for immediate public health action, but rather a signal to interrogate that point more. Could it be a data error, could it be a lab error, or is there

something going on in that jurisdiction that could explain the unexpectedly high value? Next slide.

So good that I followed Steve here. We are also looking at variant tracking through wastewater. This is not as straightforward as we had hoped.

Interpretation is limited because most of what we're detecting in our wastewater sample are fragmented genomes from the beginning because the viruses are decaying in that wastewater sample. So while we may be able to detect all 14 mutations that define something like B117, we cannot say with any certainty that all of those mutations are present on the same genome. So really, we're detecting mutations and not variants per se.

We also have some questions around method sensitivity, particularly around sequencing. So are we picking up some mutations more than others? And there's the potential for variation in shedding dynamics between variants, which can impact our interpretation of relative abundance of these different mutations.

So at this point, this is an approach that we are actively evaluating. We do believe that there is potential for wastewater sequencing to be useful for variant detection and tracking, so looking for variants of concern and variants of interest that we already know exist, but unlikely to be useful for variant discovery, again because of that problem of bringing all of the mutations together into a single genome. While we are doing this evaluation, we are moving forward to be able to bring this variant data into the NWSS system.

And so we're working with the National Center for Biotechnology Information, NCBI at NIH, to establish a wastewater sequence database that can hold all of the sequence data. It has a preliminary analysis pipeline built in so that we can get automated reporting. And all of those sequences can be linked to the wastewater sequences that are submitted to our NWSS decipher system so that we can really provide holistic analysis back to our health department partners when we feel confident in that analysis. Next slide.

So all of this was built specifically for the COVID response. But we recognized from the beginning that wastewater surveillance can really help us understand many disease targets. And so we specifically built NWSS to be an infrastructure that was flexible and would allow us to expand to multiple health targets. And we are beginning that process now to put together the first of what we're calling the NWSS panel as we expand past COVID.

We also want this to be a rapidly-adaptable system so that should another, for example, pandemic come around, we can rapidly adapt NWSS to provide that level of community surveillance that would have been so helpful in early 2020. We are still deciding what the next set of targets will be. So don't take these as set in stone. But the ones that we're thinking are most likely to be part of the next or the first round of the NWSS panel are antibiotic resistance genes, foodborne infections like *E.coli* and Salmonella, and emerging infections, like the fungal infection *Candida auris*. Next slide.

So if you want to know more about NWSS, I encourage you to go check out our website. You can either link from it here, or you can search for NWSS and CDC, and it'll take you right to it. You can also contact the NWSS team if you have any questions at nwss@cdc.gov. And if we have time and there are questions, I'm happy to answer them.

JASMINE CHAITRAM: Thank you so much, Amy. We do have time, and there are a few questions that came through when you were speaking. And two are related to safety. So I'm just going to ask them as one general question. "Are wastewater workers and environmental laboratories at increased risk from non-treated samples?" And the other question was similar to that. It was just, "Are there any safety concerns for lab staff processing wastewater?"

AMY KIRBY: Sure. So it is still a little bit of an open question how much of the virus that's detectable in stool-- so the start of wastewater-- how much of that is actually infectious. There have been some reports of successful recovery of infectious virus. But there have also been larger studies that have not shown any recovery of infectious virus. Similarly, we have seen no epidemiological evidence of infection from wastewater contact. So you might expect to see clusters with wastewater workers, and we have not seen that.

We have also commissioned a study specifically to look at potential excess risk associated with wastewater exposure through wastewater workers. And those workers, that was a six-month study. And we detected no cases in those wastewater workers despite very high exposures in the wastewater that was coming into the treatment plant, or at least very high RNA concentrations, I should say. So the overall risk from wastewater appears to be quite low, although we can't say that it's 0.

However, I will put a note on that that when we bring wastewater into the laboratory, and we want to do SARS-CoV-2 RNA testing, the first step is to concentrate those samples. So we start with a larger volume, anywhere from 20 mLs on the low end up to 500 mLs on the higher end, and concentrate that down. And those concentration

procedures will concentrate any live virus that's there. And most of them are centrifugation and things like that, that have the potential to generate aerosols. And so our recommendation for testing of wastewater in the laboratory is that it should be done in a BSL-2 plus condition, so 2 plus respiratory protection, because we think the risk there does go up from what we're seeing in just raw, untreated wastewater.

JASMINE CHAITRAM: All right, thank you. OK. Can you say again what the potential emerging infections that you're considering for future monitoring, what those are?

AMY KIRBY: Sure. So right now, *Candida auris* is the only one that is included in consideration for the version one of the NWSS panel. But we're also looking at a potential emerging AR genes, antibiotic resistance genes. We have seen this in the past, things like mcr-1, which I don't know that we can consider it emerging anymore. It's definitely here. But when we learned about it from other countries, we could have started surveillance for that here in the US. So we're thinking ahead to that type of use for NWSS data.

JASMINE CHAITRAM: OK. And are there plans to standardize wastewater testing?

AMY KIRBY: Yeah. There's been lots of discussion around that. We are still learning a lot about how these systems work. And so we have a handful of assays that work very well. It doesn't seem to be that any one is outperforming the others.

And which one is best and most applicable tends to vary by location. For example, are you in a very large utility where 5 million people are contributing to the wastewater? Or are you in a very small utility that's only 3,000 people?

We also expect that some of the methods-- what methods are performing best will change as incidence goes down. So we're keeping an eye on that as our case counts continue to decrease. So that was a very long winded way to say we don't expect to have standards in the short term. But it is something that we're looking to roll out, especially as we transition NWSS to this multi-target platform.

JASMINE CHAITRAM: OK. And then two questions that are kind of similar about if a particular state is not currently a part of the NWSS program at this time, or if there are laboratories out there that want to get involved in the initiative, how can they get involved? How can they encourage their state to get involved?

AMY KIRBY: Yeah. So our engagement with the state is always through the health department, either the state health department or the local health department, because if you want this data to be used for the response, you've got to have the health department engaged because they are the end users. So if your state is not part of it, I would encourage you to reach out to the health department and inquire with them about

why not. I will also say that you don't have to be using CDC funds and show up on that map to be submitting data to NWSS. So the health departments can still submit data even if they're using other funds to support wastewater surveillance.

JASMINE CHAITRAM: Awesome. Thank you. And thank you so much, Amy, for joining us today. There are still some questions. But in the interest of time, I'm going to move to our next speaker.

If you're able to go into the Q&A section there in the Zoom and see the questions, you're welcome to answer them by typing an answer in response. And then the other participants can also see your answer. So I encourage you to do that if you have time to stay with us. But thank you so much for joining us today and for the great presentation.

AMY KIRBY: Great. Thank you.

JASMINE CHAITRAM: And we will now move to our next topic and speaker, Linda Ricci from the US Food and Drug Administration, talking about the sodium citrate tube supply shortage. And we did send out a LOCS message about this today as well. So, Linda, would you like to go ahead?

LINDA RICCI: Thank you, yes. Thank you for including me on today's call. My name is Linda Ricci. And I'm from the Center for Devices and Radiological Health at the FDA. As you may be aware, we issued a communication last Thursday, June 10, indicating that sodium citrate tubes are experiencing significant supply interruptions in the US. As such, we have placed these tubes on our device shortages list. Our understanding is that the demand for these tubes has increased due to COVID. That has been coupled with an interruption in the supply of these tubes, which has resulted in the shortage. At this time, we expect that the supply chain will not fully recover until December of this year. However, we do expect that the situation will continue to improve between now and then.

We have suggested several conservation strategies which are also listed on our website. Specifically, we are recommending that you do not include sodium citrate tubes in routine collection of a variety of specimen at the time of other blood sampling or of IV insertion. Also, that you do not include these tubes unless it's medically necessary. Also, that you do not include these tubes as discard tubes. Instead, consider clear top or red stopper tubes. And lastly, that you limit allocation of the 1.8 milliliter tubes for difficult blood collections. FDA is recommending that labs and all health care providers develop and implement these strategies overall in order to limit the use of these tubes for situations in which it is medically necessary.

So we have sent out a notification of these conservation strategies to people that we thought would be interested in these. We also have them posted on our website and linked to our device shortages list. So trying to make this short and sweet and just make sure you were all aware of this shortage. Please let me know if there are any questions.
JASMINE CHAITRAM: Thanks so much, Linda, for joining us. And do appreciate you providing that link. And like I said, CDC sent out a LOCS message today. So if you're unsure, look in your email, and you'll find a message from CDC which will basically say the same thing that Linda just said with the link to the FDA information. I do have a question for you. Can we estimate how large of a shortage we have for the situation? What is the estimate of how long this shortage will likely take place?
LINDA RICCI: So the shortage that we are seeing right now, it's fairly severe. However, we have not heard of institutions that are not able to get supplies. If you are in that situation where you're not able to get supplies, we please ask you to contact FDA at deviceshortages@fda.hhs.gov.
Also, if there are any issues with any of the tubes with regards to a medical device adverse event, we ask you to do a voluntary report through our MedWatch program. And I'm happy to send out that information as well. As to the duration of the--
JASMINE CHAITRAM: Thanks.
LINDA RICCI: As to the duration of the shortage--
JASMINE CHAITRAM: Sorry, go ahead.
LINDA RICCI: Sure. We do expect that it will not fully recover until December of this year. We do expect that it will gradually get better between now and then.
JASMINE CHAITRAM: OK, sorry. I was going to ask you, does the FDA have any plans to do any kind of extension on the expiration date for these tubes?
LINDA RICCI: So that is definitely something that we will look into. And we're certainly looking at other mitigations for making these tubes available. And extending expiration dating is definitely something that we're looking into.
JASMINE CHAITRAM: All right, well, thank you so much, Linda. And just I've got to move to the next speaker just because we're running out of time. But if you're able to answer some of the questions in the Q&A box, I would appreciate that as well because there were a few more specifically for you about this supply shortage. And thanks for joining us today.
All right, next up we've got Tim Stenzel from the FDA, another FDA person. But Tim is a regular. So, Tim, do you want to go ahead with your update?

TIM STENZEL: Absolutely. Pleasure to join you again today. There's a few questions. I don't think I have to rush too fast, but let me know.

So the first question is, "How does the emergence of COVID-19 variants impact validity of COVID-19 tests?" To our knowledge, not significantly in any way currently. The FDA is analyzing all EUA authorized tests weekly. We have all the primaries and probe sequences. We have most, if not all, of the antigen sequences that are used for antigen and serology tests.

And so we are bioinformatically [~~INAUDIBLE~~] looking at all the indications of significance, that is either of importance or because they are prevalent, and looking at the impact. When we see an impact, we reach out to those companies. And we engage them in a dialogue about whether or not those mutations can impact performance of their tests. We've issued guidance which says that these companies should be doing this of course themselves and reach out to the FDA as needed.

So we also maintain a website, which I will put into the chat box when I'm done, for any updates. Our last update was on June 3. But again, we haven't seen anything significant. We define significant as the combined degradation of sensitivity of 5% or more. This is our measurement.

We do encourage everyone to be vigilant. And if a result does not make sense, repeat the testing with a different test. It's going to happen because of the number of mutations.

Basically, every base in the virus has been shown to mutate. And you're just going to hit some virus that will be missed by a certain test. And that's going to happen.

But we look at the impact overall from a public health perspective for any impact overall on sensitivity that's significant, not really rare or unusual cases. They can occur. And so we just all need to be vigilant.

And of course, multi-target assays are less prone to issues than single target assays.

There was a second question that was very similar. So I'm going to skip that.

Next question is, "Is a result still valid if a reagent or other testing material is substituted as an alternative when there is a supply issue?" The second part had to do with the time between collection and testing, presumably, I think, if that period of time was longer than authorized. So first thing to say is that if any changes are made to an EUA authorized test, it may change the EUA authorization status. Any changes that a lab needs to do to continue performing testing should validate that change before use, of course.

We have seen that some manufacturers of tests have gone ahead and done a comparison study between their candidate test and an EUA authorized test, only to find out later that enough changes were made to that test by the lab that rendered it not authorized. And that has presented challenges to certain test developers. It's not widespread, but it has been challenging.

We hope that there aren't widespread reagent shortages right now. And you heard about tubes. We do maintain a team that looks at shortages.

We maintain contacts with companies. We maintain contact with other agencies and departments within the federal government to look ahead and try to address these. So if you are seeing shortages that you think the FDA or others could help, you can reach out through our email address.

Next question is, "How does vaccination status impact the validity of various COVID-19 tests?" In short, it does not. The FDA has advised in a recent statement on serology testing that vaccines which of course are not made of full virus, at least not those authorized in the US, but only a part of the virus. So an immune response to a vaccine may not produce a positive result for some serology tests that don't test for that, for the antigen used, for a response to the antigen used in the vaccine.

However, if a particular serology test can detect an immune response to the vaccine, we are still unsure of what that means for protection and/or immunity. Studies are underway funded by the US government that hopefully will, in short, provide some insight into what an antibody response means. It may very well be that the antibody response needs to be measured quantitatively to know the level of antibody, to know if it's protective or provides for any immunity.

OK, the last question is, "When will labs be asked to stop using EUlA assays for COVID?" Well, as long as the emergency is declared, remains declared, EUA tests will be just fine, authorized tests would be just fine to use. There may come a time, although it's probably going to be a very long time from now, that the emergency may come to an end.

But for example, several prior emergencies are still declared for Zika and for Ebola as examples. However, the FDA is already drafting guidance, which I can't predict when that will be released, that will provide for a period of time between a time at which, say the emergency ends and at time at which assays that want to stay on the market should have achieved either a submission to the FDA of a full authorization test or have achieved full authorization. So by doing this, we want to ensure that there's an adequate supply of tests.

And of course, the supply of tests in the United States that is needed now appears to be going down. We don't know if that's going to stay that way. But we do track this carefully. And we want there always to be enough tests on the market to be able to meet the needs.

So I think that's the end of the questions, Jasmine. Back over to you. And I will put the mutation website into the chat.

JASMINE CHAITRAM: Thanks, Tim. Really appreciate that. There were a couple of questions for you. But I'm going to ask that if you can go in the Q&A box and just address those because I want to save some time for our last topic, which is the COVID-19 Viral Testing Tool.

And this is kind of, at least for some of us here at CDC, the grand finale for this call because we are very excited today about the launch of this tool. And the person who has spent a lot of time helping to develop this tool is here to demo it for us. And her name is Muktha Natrajan. And I know I didn't say that right, but we know that she's here. And, Muktha, are you on, and can you go ahead with the demo?

MUKTHA NATRAJAN: Yes, Jasmine.

JASMINE CHAITRAM: And we can't--

MUKTHA NATRAJAN: Are you able to see my screen?

JASMINE CHAITRAM: Yes, I am.

MUKTHA NATRAJAN: OK, great. I'll go ahead and get started. I'll just give a very quick 1-minute background.

I think you all are very familiar with the antigen testing guidance that also was updated recently. And this tool was developed alongside that guidance as a way to streamline some of those outcome processes to determine when individuals may need confirmatory testing related to antigen testing. The tool is also a little more in depth in that it does address results from NAAT testing as well. And it also can give suggestions for those individuals who do not have a test result but have various pre-test probability factors that might indicate that they should get COVID testing or may not need testing at this time based on current CDC guidance.

So yes, this tool is developed alongside that antigen testing guidance as well as several other published CDC guidance that are referenced and linked throughout the tool. The tool works as a chatbot. And so how it starts, you can see here there is a disclaimer related to the functionality of the tool.

And although it is asking questions about COVID-19-related factors, this is not to replace clinical judgment or clinical assessments. But it is intended for the public as well

as health care providers to use to determine if, in the case of health care providers and facility administrators, whether their patients may need further COVID testing or not, and as well as individuals in the general community and non-health care congregate settings to determine if they themselves should get some additional testing given their risk factors.

So I think what I'll do now-- this testing tool, we also have in the disclaimer, does consider vaccination and how that affects current testing guidelines as well. And of course we'll be updating as soon as we get more information on things like variants and vaccines. But for now, I'll go through just three scenarios. But we do encourage everyone-- this is currently available on the COVID-19 testing site for CDC, the main site that was also sent out in a LOCS message today.

And so one example here. So when you start the tool, you can read through this disclaimer of information. And in order to continue using the tool, you have to click “I Agree.”

And just one quick one I'll go through is if you have not received the test results. So the first question introduces you to the tool with the chatbot and asks, "If you took a COVID test in the last 10 days, what was the result of the most recent test?" In this case, someone does not have a current test result.

This is someone who lives in the community. They don't live in a congregate living setting. So they would be going down the channel of just community.

They're currently asymptomatic, but they have concern because they have not had known COVID in the past. So they don't suspect they have antibodies. They also are not fully vaccinated. So you may not have protection there.

And although they've had no known close contact, this next question here, they have been to a recent indoor event that was crowded with 100 people. And they're just wondering, should I now get a test given that exposure?

This last question asks if they have access to a NAAT if possible with less than 48 hours. Of course some people won't know the answer to that. So in this case, I'll say this person does. This is a health care provider that's saying, yes, this patient-- I know all this information about them. And they do have access to a laboratory to confirm that.

And due to that low pre-test probability in general because they are asymptomatic and have a potential suspected exposure but not known, the recommendation right now would be because they're unvaccinated and have not had COVID recently that they remain quarantined and obtain a NAAT test if possible due to that low pretest probability

and the higher sensitivity of that. But if they're not able to obtain that, still to get the COVID test in this case.

And then the final question of the tool would be, "Was this information useful to you?" And hopefully, people will say yes. But even if not, the tool leads them to contact CDC INFO with further questions as needed.

And I see that we're at a time. So maybe we'll leave it at that. But I think the overall thing I wanted to show here is that it hopefully is a quick way to really factor in several individualized factors for each person so that they can answer whether they should get testing if they don't have a result yet, or if they already have a result, whether they need confirmatory testing, whether they should isolate, whether they should quarantine.

Yeah, and thank you, Jasmine. I think I'll stop there as I see we're over time now.

JASMINE CHAITRAM: Yeah. And thank you, Muktha, and congratulations on putting together a really incredible tool. And we do hope that people visit the website, the tool, and try it out, and share it with others, and spread the word that it's available.

And apologies for running a little long today. And we just are grateful that you joined us each of these calls. And we look forward to talking to you again on June 28. Thank you.