National Government Services, Inc.

Moderator: Craig Haug, M.D.

February 24, 2022
11:39 am CT

Coordinator: Good afternoon. And thank you for standing by. And welcome to the NGS JK and J6 Open Meeting. Your lines are in a listen-only mode until the comment sessions of today's conference call. At that time you may press Star followed by the number 1 to ask a comment. Please unmute your phones and state your name unprompted. Today's call is being recorded. If you have any objections you may disconnect at this time. It is now my pleasure to turn the call over to Dr. Craig Haug. Thank you sir. You may begin.

Dr. Craig Haug: Thank you operator. Good afternoon and welcome to the NGS J6/JK Open Meeting. Next slide please. Just as a reminder the call is being recorded and transcribed, and these will be posted to our Web site in a week or two. Next slide please.

But we also welcome you on behalf of the NGS CMDs. Next slide please. The two proposed LCDs up for discussion today, or comments today, both new include multiplex gastrointestinal pathogen panel test for acute gastroenteritis and mass spectrometry testing and monoclonal gammopathy. Next slide please.

First up is the LCD multiplex Gastrointestinal Pathogen Panel, GPP test, for acute gastroenteritis. This new LCD was prompted by a reconsideration request.

Acute gastroenteritis is usually self-limiting with no recommended lab testing except for select patients such as the immunocompromised, the critically ill, and those with prolonged disease refractory treatment.

Recently multiplex GI pathogen panels which exploit multiplex nucleic acid amplification methodologies have gained traction due to reduced sample volume requirements, the potential of having a single test detect a number of organisms associated with an infectious syndrome rather than a series of individual pathogen specific assays can reduce turnaround time from days to hours facilitating earlier specific, not enteric antibiotic treatment. Next slide please.

The LCD coverage criteria on this slide describe those select patient characteristics most likely to benefit from multiplex GPP testing for acute gastroenteritis specifically diarrhea of greater than one week duration or diarrhea associated with severe illness, a high risk cost, a particular public health concern or is a separate category pre-transplant evaluation.

Contraindications include test of cure since GPPs can detect the viable and non-viable organisms, laxative use in prior 48 hours since laxatives themselves could potentially account for diarrhea, and more than 72 hours after hospitalization. Studies show that panels conducted well into hospital admission are less useful with an increased risk of accidental collateral findings. Next slide please.

In summary, studies and guidelines mostly agree that multiplex GPPs can serve as an adjunct or alternative to conventional testing. However, they also agree that the increased sensitivity of the more highly multiplex GPPs, in other words, those with more targets, can be a double-edged sword with targets of questionable clinical significance, as I mentioned earlier, even potentially non-viable organisms complicating interpretation.

The greater the target number, the greater the interpretive complexity and need for greater clinician expertise and diagnostic stewardship. Therefore, the more highly multiplexed GPPs have more stringent diagnosis, place of service and credentialing LCD requirements as detailed in the associated billing and coding article. Next slide.

We received two requests to comment on this policy. First up is Dr. Alan Wright, bioMerieux Medical Director and VP of Medical Affairs. Operator, please open Dr. Wright's line. And Dr. Wright, are you there?

Dr. Alan Wright: I am there. Can you hear me?

Dr. Craig Haug: Yes, I can. Please proceed.

Dr. Alan Wright: Very good. So I'm Alan Wright. I'm with bioMerieux. And I would like to present to you the BioFire FilmArray Gastrointestinal Panel. Can we go to the next slide?

I am an employee of bioMerieux the manufacturer of the multiplex panel. Next slide please. And next slide.

So as we know gastrointestinal infections diarrhea causes considerable morbidity in the United States and globally as a significant cause of morbidity and mortality often being in the top five causes of infant mortality in the world. Next slide please.

And with diarrhea it is important to know what is - what the condition is, what's the cause of the condition and to get the treatment right because the treatments are varied and broad ranging from antiemetics to antibiotics. And there is a risk of not getting treatment correct.

Significantly in the United States incorrect treatment can lead to C. difficile, overgrowth and infection. Also, it is important to identify as a causative agent in the case of some very contagious viruses in order to have aggressive isolation and personal hygiene. Next slide please.

Traditionally the diagnosis of infectious diarrhea has been done on what's euphemistically in the laboratory been called the stool bench, which is a wide array

of diagnostic techniques that have varying turnaround times. So the actual assembly of the whole diagnostic package extends over days due to the prolonged development of stool cultures and ova and parasites staining.

These techniques vary in their accuracy and precision, their sensitivity and specificity. And in general it's a difficult diagnostic workup to undertake. Next slide.

Again the causative agents are spread out across the different diagnostic techniques. So for the clinician it can take days in order to assemble a really comprehensive diagnostic picture. And there's ample room for improvement using this stool bench technique.

In addition, the health care system is already bearing the cost of the stool bench techniques. And what we're doing here is actually providing more modern technology to speed and streamline the diagnostic efficiency. Next slide please.

So for the physician, the physician needs an understanding of the different diagnostic techniques. This is typically a primary care illness often seen by physician extenders.

And they need to understand multiple different techniques such as the ova parasite, PCR and blood culture. In the laboratory it's expensive, it's time-consuming and it requires a high level of training actually for some of these techniques. Next slide.

So when we talk about who to test the American College of Gastroenterology recommends basically febrile diarrhea lasting greater than a week or the indications that were captured in the local coverage determination that was introduced earlier in the session. Next slide.

And what the American College of Gastroenterology also recommends is that a culture independent method should be used. And that includes FDA approved culture independent methods. Next slide.

And so allow me to introduce the BioFire gastrointestinal panel. Next slide. Here are some different colors just to give everybody a rest. Next slide.

And while the intended use is extends for multiple pages this is really the first several lines of the intended use of the FDA approved BioFire assay. It is a multiplex PCR based assay that is used on our proprietary FilmArray systems. And it's capable of simultaneous identification of nucleic acids of multiple gastrointestinal pathogens directly from stool. Next slide.

And here's a comprehensive list of the pathogens that can be identified from the FilmArray. As you can see these are common infectious pathogens found often found in the United States.

Of interest notice the C. difficile is second down from bacteria. We have the capability of turning on and off that particular marker. That is a performance marker

for hospitals, and it causes some confusion within hospitals or health care systems if they're using an antigen based test rather than a PCR based test for C. difficile.

So the clinician and the health system has the option to toggle that C. difficile on and off. Also note the superb sensitivity and specificity which is common for most PCR based testing modalities. Next slide.

It's a simple machine.The operator training is much reduced compared to stool bench. It can run in smaller hospitals. There's two minutes of hands on use as the sample cartridge is inoculated, and then it runs for about an hour. Next slide.

It is (CLIA) moderate complexity, so it does require a laboratory technician. And as I said it can run in any situation, with any moderately complex situation with a laboratorian, but it doesn't require the extreme training that's necessary for some parts of the stool (bench). Next slide.

Here's what a report looks like, and you can see it's simple, easy to read. Next slide. And the operational benefits. Next slide.

Common to most PCR based techniques the sensitivity and specificity is much higher than traditional techniques. And as noted in the introductory comments it still needs a clinician interpreting this.

There is the possibility of PCR to detect nuclear fragments rather than actual infectious entities so we always recommend the use of this test with - in conjunction with a thorough history and physical.

And that really concludes my comments for today, so thank you for listening. Next slide. I'm Alan Wright, and I'm with bioMeriuex.

Dr. Craig Haug: Dr. Wright, thank you for these comments.

Dr. Alan Wright: You're welcome.

Dr. Craig Haug: Next slide. Our next comment is Dr. Matthew Binnicker, Director of Clinical Virology at Mayo Clinical. Dr. Binnicker are you able to speak?

Dr. Matthew Binnicker: Yes, I'm here. Can you hear me?

Dr. Craig Haug: Great. I can hear you just fine. Please proceed.

Dr. Matthew Binnicker: Excellent. So thank you for the opportunity to speak on this important topic. I'm Dr. Matt Binnicker. I'm the Director of Clinical Virology at Mayo Clinic in Rochester, Minnesota.

And I'm speaking on behalf of our team and the Division of Clinical Microbiology and Infectious Diseases at Mayo Clinic on this issue of appropriate use of Gastrointestinal Pathogen Panels for evaluation of acute gastroenteritis. And we definitely agree with the approach of making sure that there's judicious testing and that the testing be performed in the appropriate setting in the right cases.

Just a quick word on Mayo Clinic and our laboratories. We perform testing not only for our patients that are seen in hospitals, emergency departments, outpatient clinics, but as well we receive samples from all over the United States through our reference laboratory including patients who are evaluated at other locations for acute gastroenteritis. Next slide please.

Just a correction on this slide. I am an Advisory Board Member for DiaSorin Molecular. I haven't received any personal funds from any company that manufactures Gastrointestinal Pathogen Panels.

And I'd also wanted to underscore that in 2014 our labs at Mayo Clinic did evaluate the FilmArray gastrointestinal panel, and we received reagents from BioFire to perform that study, which is published in the Journal of Clinical Microbiology. Next Slide.

So our team is definitely appreciative of these guidelines and agrees with the overall theme of ensuring judicious use of these tests especially the clarification that these tests can be used when community acquired diarrhea of at least a week's duration is present, which is common in our general population. Next slide please.

One point that we do think requires further discussion is the guidance's requirement for an independent laboratory to be able to be performing the test only in a situation where there's a pre-transplant evaluation or an individual with an immune compromised condition. In our practical experience, other than the emergency department, it's the outpatient setting that's most appropriate for Gastrointestinal Pathogen Panel testing and where the majority of patients with at least a week of diarrhea are seen.

Our primary care providers are the usual ordering and treating physicians for these types of patients who present with at least a week's duration of acute gastroenteritis and not our infectious diseases or specialty care. Our primary care providers definitely can reach out and consult with specialists in infectious diseases or other specialties who can help with interpretation and treatment decisions, but it really is our primary care physicians in the outpatient settings who are seeing these patients.

And I think because of the number of patients who present with a week or more of acute gastroenteritis there simply aren't enough infectious disease specialists to require that all of these patients be seen by the specialists for this type of testing. So use of the Gastrointestinal Pathogen Panel we feel allows for best use of health care resources because identification of the causative agent of the acute gastroenteritis can help tailor therapy and prevent downstream complications such as dehydration that can lead to patients ending up in the hospital as well as other adverse outcomes.

So again allowing outpatient primary care physicians the ability to order and treat based on the findings we feel will lead to decreases in downstream hospitalization and inappropriate treatment decisions. Next slide please.

So our specific request is to allow Gastrointestinal Pathogen Panel testing to be performed in independent laboratories beyond the setting of a pre-transplant evaluation or in an immunocompromised host. For example, testing by primary care providers allows for identification of the causative agent in patients with a community acquired diarrhea of greater than one week's duration.

And as I mentioned earlier most of these patients are unlikely to be seen by a specialist such as infectious diseases within a week of their symptom onset because there simply aren't enough infectious disease specialists to see all of these patients. And it really is our primary care physicians who are going to be seeing the majority of these individuals with persistent diarrhea.

Our second request is to include ICD-10 codes for unspecified diarrhea and infectious gastroenteritis and colitis. Next slide please.

So with regards to the ICD-10 codes those should include diarrhea unspecified with the R19.7 as well as infectious gastroenteritis and colitis. Next slide please.

So I just again want to thank the panel for the opportunity to present today and to share our perspective on this important topic. And I'll look forward to the discussion. Thank you.

Dr. Craig Haug: Dr. Binnicker, thank you for your comments. And before we move on I have a question for you. As you know the GPPs come in different flavors in other words different levels of targets.

In fact there are three codes, not including the PLA code, that govern this, you know, one up to five targets and six through 11 and over 11. The current policy doesn't have those restrictions you mentioned on the less than five, it does on the greater than five.

And so are you saying a primary care clinician, or as Dr. Wright mentioned even a physician extender, should be able to order without consultation any kind of highly multiplexed GPP one with a couple of dozen targets on any patient with over a week of diarrhea?

Dr. Matthew Binnicker: Yes, that's our position.

Dr. Craig Haug: Or I guess the follow is or should the primary care provider know when a five GPP would suffice? That's really the crux.

Dr. Matthew Binnicker: So our position is that the majority of patients who have diarrhea of a week or more duration are going to be seen by primary care providers in the outpatient setting. And that we feel it's appropriate to order a test that may have 15 to 20 targets to cast the broad net and assist in diagnosis and appropriate management.

In speaking with our infectious diseases colleagues, here at Mayo Clinic, they confirmed again the majority of those patients are seen in the outpatient setting by primary care providers. And that in the situation where a pathogen is detected and

there are questions about appropriate management and treatment here at Mayo Clinic those primary care providers then reach out and have discussion, sometimes with infectious disease specialist.

Other times if based on experience and prior utilization of these panels that they may not reach out to infectious disease specialists depending again on their experience level and comfort with treating such conditions.

Dr. Craig Haug: Would you ever recommend that a GP with only five targets be used?

Dr. Matthew Binnicker: I think it's possible that in certain scenarios where there's maybe a more clear indication of which causative agent may be responsible for the infection that smaller panels may be appropriate. But many of these situations it's very unclear, and the differential can be quite broad.

And I think in those situations targeting a larger number of potential pathogens makes sense. And so again it really depends on the patient and the situation, maybe their exposure histories to determine whether starting with a smaller panel initially would make sense or starting with the broader panel.

Dr. Craig Haug: And last question, in that outpatient setting, the primary care physician extender, what percent of the time, just as a ballpark, would you say that they actually reach out for consultation on whether to order, you know, highly multiplexed GPP that, you know, does complicate the interpretation?

Dr. Matthew Binnicker: Yes, since these panels have been used now for at least five years in many settings I think the comfort level within the primary care setting of getting these types of results back and treating such conditions has improved significantly. So there's probably a lower percentage of situations.

If I were to estimate maybe 25% of situations where primary care providers may need to reach out to an infectious disease specialist for help with interpretation. But many of these primary care physicians have now encountered these types of situations, in the past have talked with colleagues about how to interpret and treat. And so I think that percentage of time where they have to reach out for help with interpretation is over time decreasing.

Dr. Craig Haug: And I know I promised just the last question, but your response made me think of another one. So that's mostly on the back- end the interpretation?

Dr. Matthew Binnicker: Right.

Dr. Craig Haug: What about the ordering? Do they ever reach out before they even order one of these or is it pretty much a reflex towards BioFire FilmArray at this point?

Dr. Matthew Binnicker: Yes, I think in some situations they may reach out, but I think the rate of that happening is probably much lower today than it was five, seven years ago. Again, based on the experience, the fact that these types of tests have been around and

used more frequently, the comfort level within our general primary care physician population is much higher today.

And so I think the rate of reaching out before ordering has dropped significantly. And I don't think it occurs in many situations.

Dr. Craig Haug: Okay, thank you again for your comments and the conversation. Operator, can we see if there are any other comments on this policy?

Coordinator: And if you do have any comments you may press Star 1. Again, for any comments please press Star 1. I am showing no comments.

Dr. Craig Haug: Okay, any comments on this policy for this open meeting are now closed. Next slide please.

The next policy up for comment is mass spectrometry testing in monoclonal gammopathy. This new LCD is also instigated by a reconsideration request.

Monoclonal gammopathy is characterized by the proliferation of a single clone of plasma cells which produce monoclonal immunoglobulin proteins, so-called M proteins. Currently suspected monoclonal gammopathies are initially detected using a combination of three serum based diagnostic tests, protein electrophoresis, immunofixation electrophoresis and measurement of free light chain.

The idea behind mass spectrometry is that molecular mass can be used instead of electrophilic patterns to identify and quantify M-protein since each light and heavy chain has a unique amino acid sequence and thus a unique molecular mass.

In theory this unique mass can be used to generate mass spectra from which MPs could be identified, isotyped and quantified. Next slide, please.

The LCD coverage criteria on this slide and describe those patient characteristics most likely to benefit from mass spectrometry testing as a potential alternative to one of those three tests the serum immonfixation electrophoresis in monoclonal gammopathy, both in the context of diagnosis and monitoring. Next slide please.

In summary, NGS considers serum mass spectrometry use in monoclonal gammopathy as a potential alternative to serum immonfixation electrophoresis in confirming a serum protein electrophoresis or serum free light chain abnormality, the other two of the three that I mentioned.

Largely in concordance with the very recent College of American Pathologists, CAP, American Association of Clinical Chemistry, AACC, and American Society for Clinical Pathology, ASCP Collaborative Guideline. Next slide.

We received one request to comment on this policy, that from Dr. David Murray, Co-Director of Protein Immunology Lab Mayo. Operator can you open Dr. Murray's line please?

Dr. David Murray: Hello, can...

Dr. Craig Haug: Dr. David Murray can you...

Dr. David Murray: Are you able to hear me?

Dr. Craig Haug: I can hear you sir. Yes, we can hear you, please proceed.

Dr. David Murray: Okay, can you go to the next slide, please? As a way of introduction - this is different.

Okay, so I'm David Murray. I am one of the inventors on a patent that was granted on this for full disclosure. And I also should say I was part of that guideline that you just mentioned from CAP and AACC. I was the AACC member on that.

Mayo has received patents on this. And they've been licensed to a company called the Binding Site, who is developing this into a clinical assay. All right, next slide please.

So I guess this was the question, why did we set out to do this mass spec test when protein electrophoresis and immune electrophoresis has been used so well over the years? I'm going to try to attempt to answer that in this next slide. Next slide please.

So what we know thankfully survival of myeloma is increasing from about eight months in the 1950s to over ten years currently. And now with the new treatments more and more patients are getting to lower levels of disease which means they get to these lower M-protein levels that are detected by the electrophoretic methods.

And these electrophoretic methods, as we find, are really not capable of detecting these lower levels of disease. So what's been going on is the labs are now switching to going in to get bone marrow biopsies and trying to evaluate the level disease which is quite more expensive than electrophoresis and painful. So our thought was could we make a more sensitive serum based test that would be better for the patients?

In addition to that one of the reasons these diseases are improving is there's a new class of drugs which we call therapeutic monoclonal antibodies, which can interfere with the detection of monoclonal antibodies secreted by the plasma cells. And that little graph down there just shows you on the left when we compare normal IFE in the blue to the new, what we're calling a mass fix test here at Mayo, in the green.

And as we dilute these patients who have these monochrome proteins in the normal human serum you can see that we are able to detect the residual monoclonal antibody or related to the disease at a higher level than we could by IFE. And on the right it's just an example of a patient who has a Walden strom’s Macroglobulinemia and is diluted in the normal human serum. And the mass spec is able to detect it at much lower levels.

And I've included on the bottom, just for your interest, some of the benefits that we've published. The first publication is really talking about how we can use the mass of the monoclonal drug once we measure that to helps discern the difference between the drug and the patient's M-protein.

The second one is showing how this increased sensitivity of detecting monoclonal proteins by mass fix is really helping to do prediction of disease free survival. And the last one is another one where we looked at the progression free survival, overall survival in a multiple myeloma trial called the STaMINA Trial. And it showed that the mass spec was better than IFE doing that. So that's why we're doing that. Next slide please.

And the other thing that's happening in the field is this new sense of what we call monoclonal dermopathy of clinical significance. And these are usually low level M proteins certainly in the MGUS range that we're seeing are now related to symptoms in patients.

So the rule of low M proteins and renal failure. There's a new entity called monoclonal gammopathy of renal significance. There's an entity called PGNMID which shows monoclonal deposits in the kidney. Of course AL Amyloidosis and light chain deposition disease these are all diseases that usually are associated with very low M protein levels.

Also, the rule of low levels of M proteins in peripheral neuropathies (POM)s is just one example. But now there's a whole series of diseases related to our IgM monoclonal proteins called the IgM related neuropathies.

And most recently now after the vaccine for COVID has come out we've seen that these vaccines induced thrombosis in patients is also due to a low level M protein. And the role of M protein light chain disglycosylation which has the only kind of been recently discovered using the mass, as we can see the mass shift with disglycosylation and its role in cold agglutinin disease. And the references for each of those are there if you're interested. Next slide.

So here are some of the requests from Mayo. We know that the urine testing wasn't covered but our code 0077U unfortunately has both serum and urine in it. And we realized that, you know, we wanted - that you suggest a document in which one we were using when we did the test.

But actually Mayo is in the final stages of validating a urine IFE replacement using mass spectrometry. We'd be happy to share that data with you if you want because we just submitted it for New York State approvals just yesterday actually.

We've published data showing that equivalency of urine mass spec was urine IFV. And the urine data is used in diagnosis and response criteria for myeloma and amyloid patients. I would say that urine doesn't have the same diagnostic value that it did many years ago, but I think it's still mentioned in the guidelines for detecting some of these low level diseases.

So if that is allowed then we would request that the urine testing coverage, the documentation of which we did with would no longer be needed. And this was details I got from our financial billing people of the details in the claim. And then the PLA code could be billed twice per day of service if that happened because we could run serum and urine on the same date of service. Next slide please.

This just shows that there's still some urine recommendations by CAP and the IMWG. I put those in the new guidelines and I put the tables where the urine is mentioned.

And also in evaluating treatment response, and this is somewhat critical because if a patient is not considered in strict complete remission then they're less likely to do all the high sensitivity flow on the bone marrow. So we feel like we could limit the number of cases that have to go to next generation sequence and high sensitivity flow for MRD testing.

And the next point, bullet point is basically we just publish this data in one of our publications. And the references there on the side. And Table C just shows that the data that we did comparing urine IFE and urine mass spec. Next slide please.

And the other request we have is we would like to ask that serum and urine is not only limited to the myeloma indications, we looked at the indications in which we currently bill this test under and neuropathies are one of them. And that's really to look for Poland syndrome and AL Amyloidosis is also part of the neuropathy symptoms.

And here at Mayo we see it quite a bit of amyloid patients. I would say half of our patients under treatment now are amyloid. And these sort of patients who come to Mayo with nonspecific symptoms, neuropathies are one of them. And so when they come here we tend to order a lot of these monoclonal gammopathy testing to rule out those diseases.

Same thing true for chronic kidney disease. That's because of the entities I've described. And then skin rashes because we do cryoglobulinemia which is a monoclonal protein, can be a monoclonal protein related disease. We're asking that be considered as another reason to order the test.

Heart failure, mostly due to AL amyloidosis, so you get really restricted cardiomyopathy. And so those codes are sometimes used.

And sometimes we see that the symptoms for myeloma are also ordered like unexplained anemia, unexplained high levels of immunoglobulins or thrombocytopenia now because of the relationship of low level M proteins with that. Next slide please.

And this just as a reminder. This is what we've been currently billing for many years, at least that I've been in the lab. And you've already reviewed those and you can see that CPT codes that are associated with that.

But what I wanted to point out is what we're really asking for -- next slide please -- is not increased - we're not adding new tests, we're really simply replacing serum immuno fixation with serum isotyping with this PLA 0077U. And we have been running urine immuno fixation for years and we'd like to replace that also with this method because of the benefits for the patient. Okay, next slide please.

And with that I'll stop and take any questions you might have.

Dr. Craig Haug: Dr. Murray, thanks for those comments. I have a couple of questions. You mentioned billing both the serum and the urine, so billing 0077 twice.

I think I recall a study that looked at using both and I think it increased the sensitivity somewhat. Is that the reason for what might otherwise seem like somewhat duplicative testing?

Dr. David Murray: Yes.

Dr. Craig Haug: So would then two tests be the default going forward if that were the case?

Dr. David Murray: Well yes. So one urine is tricky. So what you typically see in the urine or just the light chains because the, you know, the barrier of filtration in the kidney cutoff around 60,000 daltons. So impacted immunoglobulins can be held back where the light chains will pass right through the kidney.

And so where the urine really comes into benefit, and its sensitivity, are things that are associated with free light chains and that's primarily AL amyloidosis. And if you look at those guidelines that were put out one of the indications - the only really indication to order urine for a diagnostic criteria is if you're really looking for these low level diseases like AL amyloidosis or lysine deposition disease.

So, you know, plenty of patients who have MGUS where we can detect the monoclonal protein in their serum and will not have any findings in the urine because they don't have damaged kidneys. And that large protein can be held back by the kidneys so we only pick up the monoclonal protein in the serum but we really don't need to do urine in those cases.

So according to guidelines the only time you really should use urine for diagnostic criteria is if you're thinking of AL amyloidosis. Now, I know that's probably over ordered for other reasons than that but I know here at Mayo that's one of the reasons that we do urine on patients.

Dr. Craig Haug: So the dual testing you'd recommend only in the setting of suspected AL amyloidosis?

Dr. David Murray: Yes, that's where we recommend it or urine is still used in the response criteria to treatment for myeloma also. So that's the other indication where it gets ordered.

There's a big push in the International Myeloma Working Group right now we're trying to get - we're thinking maybe it's time to try to get urine out of this whole

response criteria and stick to this MRD testing. But that hasn't happened yet as I'm reminded by my colleagues.

Part of getting and the criteria to do the bone marrow testing for, for minimal residual disease is that the patient has to be in strict complete remission. And that requires a negative urine that there's no disease in the urine.

So urine gets ordered quite a bit in order to stratify those patients on who gets MRD testing and who doesn't. And it's also required in drug studies right now is that most of the trials are requiring urine also. But there is a big push to try to push to get it out of the testing right now.

Dr. Craig Haug: Okay, thank you. And would you say that the collaborative guideline, that we both referenced, does that include endorsement of urine testing for certain indications?

Dr. David Murray: Yes, it says in their urine if you suspect AL amyloidosis. I think I put the table where I've pulled it out of, but I was part of drafting those guidelines.

Dr. Craig Haug: Okay. And did they, similar to others, talk about the - so they referenced them. I'm trying to see if they say or - I mean and again we're talking about this as a basically replacement for immuno electrophoresis IFE as the guidelines say that that should be used to confirm the SPEP or SFLC abnormality use IFES IFE, so serum, or an alternative method with similar sensitivity, and they do talk about the mass spectrometry. Is there something similar to that where they say they really point to urine spectometry testing as an appropriate alternative?

Dr. David Murray: Yes, we didn't - in the guidelines we didn't do that because we hadn't finished all of our validation studies at that time.

Dr. Craig Haug: Okay.

Dr. David Murray: But yes, so it's not like I'm - I was trying to say we're not trying to add on to the testing here it's just we're going - we're planning on replacing what we used to do with gel electrophoresis with urine with mass spectrometry. So we're not adding anything new to the guidelines we're just replacing one test with another that's...

Dr. Craig Haug: Yes, yes. Okay, and you mentioned something - some validation work that's about to be published I think?

Dr. David Murray: Well, yes, well we did it internally. So we did - we developed this as a lab developed test so we have the, you know, CLIA guidelines. We did that.

And then we sent that in order for us to get permission to bill this to New York State we have to send our validation data to New York State. So that's what we're doing now. We're in the process of sending that validation. And we are planning on publishing all of our results but we haven't done that yet.

Dr. Craig Haug: Okay. Again, Dr. Murray, thank you for your comments and this discussion. I appreciate it.

Dr. David Murray: Thank you.

Dr. Craig Haug: Operator, are there any other comments on this policy?

Coordinator: Once again if there are any comments you may press Star 1. And sir at this I am showing no comments.

Dr. Craig Haug: Okay, then comments on this policy for this open meeting are now closed. Next slide please.

This slide shows the official comment period ending on March 26, 2022. Next slide. And this is where to send the email or snail mail. And also please note that the conflict of interest requirement. So anybody who sends in a comment please include your conflict of interest if any.

All right, so this concludes our NGS J6/JK Open Meeting. Thanks, everybody for commenting and attending. Have a good day.

Coordinator: Thank you. This concludes today's conference call. You may disconnect at this time.

END