First Coast Service Options, Inc.

Medicare Administrative Contractor (MAC) combined JH/JL/JN contractor advisory committee (CAC) meeting

Thursday, October 6, 6 p.m.

Topic: Molecular testing in infectious disease

MAC Participants

Leslie Stevens, MD - Novitas Solutions Executive Contractor Medical Director

Patrick Mann, MD - Novitas Solutions Contractor Medical Director

Suzanne Kim Doud Galli, MD, PhD – Novitas Solutions Contractor Medical Director

Juan Schaening-Perez, MD - First Coast Service Options Executive Contractor Medical Director

Alicia Campbell, MD - First Coast Service Options Contractor Medical Director

CAC Member Panelists

Terrence Regan, MD - Urology

Hema Kapoor, MD - Infectious Disease

F. Wilson Jackson - Gastroenterology

Alfredo Vazquez-Sandoval, MD - Pulmonary Medicine

Scott Manaker, MD, PhD - Pulmonary Medicine

Evan Pollack, MD - Internal Medicine

Mark Block, DPM - Podiatry

Raul Benavides, MD - Pathology

Jeffrey Kwong, DNP - Nurse Practitioner, Infectious Disease

Bryan Youree, MD - Infectious Disease

Meeting

Mandy McGarvey

Welcome and good evening. My name is Mandy McGarvey, and I'll be your Webex host for today's Novitas and First Coast Contractor Advisory Committee meeting on molecular testing in infectious disease. Before we get started, I did just want to take a moment to remind everyone that this meeting is being recorded. CMS requires all MACs to record each CAC meeting and maintain them on their respective websites. By remaining logged in and connected via webinar, you acknowledge that you have been made aware that this CAC meeting is being recorded, and you are consenting to that recording. If you do not consent to being recorded, please disconnect from this virtual CAC meeting. Otherwise, your continued connection to this meeting constitutes your consent to this recording. This meeting is open to the public to observe. And CAC members participating in today's meeting have signed conflict of interest and disclosure to publish forms on file. At this time, I'm going to go ahead and turn things over to contractor and medical director Dr. Patrick Mann.

Dr. Patrick Mann

Good evening, all, and thank you very much to our CAC members for volunteering and participating in this review of the questions we have regarding molecular testing in infectious disease. I believe we have to introduce some of-- I believe we have some other people here at the meeting to introduce. So also, in the background, listening with us is Dr. Leslie Stevens, one of our two executive CMDs, as well as Juan Schaening-Perez, our other executive CMD. We also have Alicia Campbell and Suzanne Kim Doud Galli, in addition. Next slide. We would also like to introduce the CAC member panelists that are with us today. We have the list shown here. I will do the best I can to pronounce names. Again, I apologize if, with some names, I do not pronounce them correctly and will definitely take advice on how to pronounce them correctly when we hear them speak. So we have Dr. Raul Benavides from pathology, Dr. Mark Block with podiatry, Dr. Michael Crossey with pathology, Dr. Jack Griebel with infectious disease, Dr. F. Wilson Jackson with gastroenterology, Dr. Hema Kapoor with infectious disease, Dr. Jeffrey Kwong as a nurse practitioner.

Next slide, please. Dr. Scott Manaker with pulmonary medicine, Dr. Charles McWilliams with urology, Dr. Benjamin Mena with internal medicine, Dr. Irving Nachamkin with clinical microbiology, Dr. Evan Pollack in internal medicine, Dr. Kenneth Rand, infectious disease, Dr. Terrence Regan with urology, Dr. John Reindhardt with infectious disease, Dr. Michael Ruzek with emergency medicine, Dr. Ray Sukumar with pathology, Dr. Kaede Ota Sullivan with clinical microbiology, Dr. Alfredo Vazquez-Sandoval with pulmonary medicine, Dr. Howard Waksman with pulmonary medicine, Dr. Bryan Youree with infectious disease. And the purpose of today's meeting is to discuss infectious disease testing panels from the molecular angle, namely testing for DNA and RNA related to infectious disease. And some of the topics that we would like to expound upon include what would be the appropriate size for a molecular infectious disease panel, what subgrouping do we need to consider when developing guidelines and policy when discussing the various subcategories in infectious disease and what molecular panels apply, and then what progress has been made and is being made in the field and how to address this in policy, especially with a mind towards being comprehensive to the future.

The meeting today is to gain observations and expertise from our CAC members, who represent a wide variety within the fields that would be using the molecular infectious disease testing. We also would like to look at the clinical uses within a particular population, namely the Medicare population, understanding that molecular infectious disease panels can represent a variety of different populations, not all necessarily representative of the Medicare population, and with the mind towards improving health outcomes in the Medicare population. And finally, the overall part of this meeting that we want to get to is whether or not a local coverage determination is necessary or are policy documents necessary to clear up clinical expectations for billing infectious disease for Medicare. Next slide.

So just as a brief introductory background to some of the things that we are seeing in the field with infectious disease that are of concern and we want to discuss more at length. We're seeing a very significant increase in the utilization of molecular infectious disease panels. And one of the things that we see is there's a little bit of confusion in terms of how to code these tests properly, with some codes being unbundled, so having multiple codes billed for a single test as opposed to one code billed for a test. And then sometimes we're seeing unnecessary repeats of codes or tests for molecular testing in particular.

One of the things-- the most common categories we see kind of coming through our system are molecular panels for UTIs, urinary tract infections, wounds, gastrointestinal infections, and respiratory infections. Additionally, we've noticed both conversation and developing testing directed in regions such as the microbiome or metagenomics. And we'd like to understand more about these, seeing as they are becoming increasingly discussed and applied to clinical medicine. And finally, we're also interested in industry standards, namely guidelines, sources, reference materials that can further back the recommendations that we hear today to help us gather the peer-reviewed literature to further clarify what we are talking about. Next slide. Oh, there we go. So the bibliography is also included. There's 100 articles from various authors that we found in our review of the current body of literature. And many of these articles come from already existing gastrointestinal and respiratory panel LCDs that have already been put in place. These questions that we are going to discuss, as well as the literature, have been provided to our panelists as of September 1st of this year. And they can also be found posted on the Novitas and the First Coast websites.

And with that, let us begin our discussion with our panel of experts. And once again, thank you for all that are here to participate in this. Our goal during this meeting is to facilitate both a lively and thorough discussion of the questions. We wish to hear from as many different angles as we possibly can for all stakeholders that use the molecular testing and the benefits that it provides towards Medicare patient care. As we move through the questions, we ask that you raise your hand virtually and then accept the invitation to unmute your mic once prompted to do so, so you can make a comment. We also encourage open dialogue and discussion to share your thoughts and to share your thoughts on each other’s thoughts through the meeting and to really get into the questions as much as we can to flesh out what we want to express about them.

Also, if there are questions from anything other than the Medicare Part B, that's not going to be covered in this discussion. We are not discussing patient care for those who are ill enough to be admitted to the hospital, which we recognize is a entirely different clinical paradigm in this discussion. So we will be only discussing Medicare Part B perspective. And with that, let us start off with our first question. The first question we had for our panelists was, what are the steps of clinical decision-making that lead to ordering a molecular infectious disease panel? And as a sub-question to this larger overall question we want to discuss, are there any particular uses for protocols for molecular testing in the context of antimicrobial stewardship?

[silence]

Dr. Terrence Regan

Hi. This is Terry Regan. Thanks for convening this CAC meeting. I think it's very appropriate. I'm a urologist. I practice in Florida. For this first question, in our own group, Advanced Urology Institute, we have our own protocol on when to use molecular testing. And the reason we do that is that we don't think that it's necessarily needed for the primary workup of urinary tract infection and primarily should be reserved for those who have recurrent urinary tract infections, complicated urinary tract infections, persistent urinary tract symptoms with negative cultures because I think, really, this helps us identify those patients who may have polymicrobial infections or haven't been picked up on previous cultures. 40% of urine cultures will be negative but will be positive with the molecular test, and it can be quite a dramatic result for the patient. In terms of antimicrobial stewardship, the problems that we have in neurology, and probably in a lot of different fields represented today, is that quite a few patients are sent to us who have already been on cycle upon cycle of antibiotics. And many patients are just randomly chosen to be put on antibiotics. And molecular testing can help us significantly identify what are the microbial agents that are causing these infections and treat them appropriately so they can get off the so-called antimicrobial merry-go-round.

Dr. Patrick Mann

Thank you, Dr. Regan. So I'll ask some follow-up questions after this, some time for discussion, as I want to let you guys discuss things. So let's hear from Dr. Kapoor.

Dr. Hema Kapoor

Hi. Good evening. I'm representing ACLA. And from the reference laboratory perspective, our thinking is that the provider who has the patient in front of them can have a best approach for clinical decision-making, like what molecular test or panel they need to order, because they may see different clinical presentations for respiratory tract infections or, as Dr. Regan mentioned about the UTI, whether it's complicated or uncomplicated. And then the same thing for the gastrointestinal, whether it's a chronic diarrhea. But regarding the follow-up question, I think the timely education we provide to our clinicians who are using the appropriate molecular panels is because it can help them differentiate between the viral versus the bacterial. And that's where is the key point. If they have a diagnosis that it's definitely a viral pathogen, then they don't need those antimicrobials in those patients, which may happen in the case of the empiric use of the antibiotics.

Dr. Patrick Mann

Thank you very much, Dr. Kapoor. Let's hear next from Dr. Jackson.

Dr. F. Wilson Jackson

Yeah, hi. Again, that you for convening. This is a terrific opportunity and thank you. I'm just going to build on the prior two comments. I'm a clinical gastroenterologist in the state of Pennsylvania, representing the Pennsylvania side in gastroenterology of the state GI society. So it's an opportunity to kind of canvass our membership and just kind of filter some-- or funnel some feedback to the group. Similar to the colleague down in Florida, the urologist, within our practice, we have criteria for appropriate use of the PCR-based testing. Acute bloody diarrhea is something we feel is important to identify the infectious organism to help guide management. And then also, protracted diarrhea, greater than six weeks, where there's potential risk factors of infectious pathogens. Travel, for example, other potential exposures. I would like to say that the question of C. diff is a separate entity unto itself, and it has its own challenges. Within our practice, we do not use the PCR testing to follow up on C. diff management or treatment. It's just simply too sensitive for those purposes, so we've not done that. In fact, we had challenges convincing patients that this is not the test to order. But I think the critical part is antibiotic stewardship, as you mentioned, appropriate use of antibiotics. And if it's a viral pathogen that you can identify quickly, those people just don't need antibiotics. And oftentimes, it's just management based on symptoms and hydration status. The luxury and the convenience of this test is, oftentimes, that we have an answer before the patient walks out of our clinic, which is a terrific opportunity compared to the conventional measures of sending stools out, which is fraught with all sorts of kind of errors along the way.

Dr. Patrick Mann

Thank you, Dr. Jackson. I don't see any other hands right away, so I do have a couple of questions that I'd like to throw out there both for the people that have already spoken as well as any future people that are speaking. So what I'm so far hearing you all say is that the clinical decision-making has, in part, to do with the antibiotics and trying to decide whether or not this is a viral or bacterial infection. And in the outpatient setting especially, it's very convenient to have the rapidity of the test results available. What I also hear is that with, for example, the UTIs, the concern is largely centered around repeated testing that doesn't either resolve the issue or doesn't discover the causative organism and that the molecular testing provides a higher level of sensitivity to detect these organisms and treat them appropriately. One of the things that I would like clarification on, if I may, is the question of, are these internal hospital protocols? Is there a certain threshold that must be passed before a molecular test is ordered as opposed to some of the more traditional testing modalities, like urine cultures or stool cultures or a parasite analysis? So if anyone would be willing to speak to that, that would be great. I see several hands. So we will start at the top of what I'm seeing on my list. And it is Dr. Vazquez first.

Dr. Alfredo Vazquez-Sandoval

Yeah. Hello. My background is pulmonary medicine. We do have protocols in the inpatient side but not in the outpatient side. I think it has become a reflex test that people order whenever they're ordering cultures for any patient that's getting a bronchoscopy for a possible pneumonia in the outpatient side.

Dr. Patrick Mann

Can you clarify what you mean by reflexive? So in the outpatient—

Dr. Alfredo Vazquez-Sandoval

I said—

Dr. Patrick Mann

--you said it was-- reflexive to what?

Dr. Alfredo Vazquez-Sandoval

No. I think it's just physicians. They're saying, basically, "If I'm trying to rule out an infection, I know that I'm going to get-- I want to rule it out with the usual culture. But now I have this test available," and it just gets ordered. As you guys know from the literature, in the outpatient setting, there's nothing really prospective or randomized to say that these things may or may not help.

Dr. Patrick Mann

Thank you very much, Dr. Vazquez. Let's go with Dr. Manaker.

Dr. Scott Manaker

Thanks, Dr. Mann. And thanks for the opportunity to participate tonight. My comment is more of a question so that I make sure I understand the framing of our discussion because in your posing of the question, you mentioned hospital protocols. And my understanding is really excluding inpatients. So the first question is, was that a slip of the tongue, or were you referring to hospital lab protocols for processing or not processing specimens from outpatient sites where the specimens were obtained? And then, secondly, when you speak to Part B, should our discussion have any site of service restrictions? Are we talking about the office setting? Are we including or excluding emergency room assessments for patients who are discharged home? Or are we including a discussion of testing and the propriety of that testing for patients being held for observation services where there's clearly going to be enough time for a test taking a couple of hours to come back and inform that patient's care? Is it limited to any of those sites of services?

Dr. Patrick Mann

Those are excellent questions and thank you for bringing them up. As for the hospital thing, that was probably an imprecise term. I know that hospitals can also include emergency room and other Part B settings as hospitals both include outpatient and inpatient clinics. But as to the answer to the second question, we really do want to cover anything that would be billed in Medicare Part B, which would include office and some of the other sites that you were discussing. What we're trying to avoid is that we know that when a patient is sick enough to be admitted from inpatient all the way up to the high-level inpatient, like ICU, the testing paradigms are very different and require a very different set of analyses and protocols. But we're trying to address the patient that is in the outpatient setting.

Dr. Scott Manaker

Okay. So outpatient, outside of the facility. Not sick enough to be receiving observation services, not sick enough to be referred to the emergency room, really the physician office side of service.

Dr. Patrick Mann

Well, I would have to clarify that I think that, in this case, we would be thinking in terms of the way that the Medicare policy is broken apart into Part A and Part B, which have entirely different coding systems. So I do understand that it's a little bit administrative in terms of the categorization, but that's, in part, the limitations that we have in terms of describing what needs to be discussed, if that helps any.

Dr. Scott Manaker

I'm not sure, but I think it provides us at least a sufficient framework to continue the discussion.

Dr. Patrick Mann

Okay. And also, some of my fellow CMDs, they are clarifying that observation, B of A, would be in the scope of this. Again, it's in the Medicare B realm that we're looking at. So the observation would be falling within this. Again, we're just trying to avoid discussions about these very sick patients that are admitted into the ICU and falling under the Part A Medicare umbrella.

Dr. Scott Manaker

Right. Well, I'm glad for that clarification because while we could probably have a debate about the utility of molecular testing for outpatients where we'd like a diagnosis to help our antibiotic management but it's clear they're not sick and we're going to be sending them home, I think that's different in the patient that we're sending to emergency department or sending in for observation services, where there is a much higher frequency perhaps of co-infections with multiple viral pathogens, higher frequency of immunocompromised patients where the diagnostic testing becomes clinically far more important in those populations in the emergency room and receiving observation services. So I would have a much lower threshold for covering these kinds of tests in those settings, those sites of service. Thanks.

Dr. Patrick Mann

Well, thank you. That clarification, I think, helps us all. So I appreciate you bringing that up and making sure that we clarify that for you. Also, consider the emergency room is, again, another B of A, a medical Part B of A situation. Let's move on to Dr. Pollack. And I think we have time for him as well as maybe two more. And then we should probably keep moving through the questions. Again, I want to reiterate that if we don't have time to get to your input and/or questions, we ask that you please do submit in writing following the meeting to Heidi DeDay to capture all the information that you wished to provide. Dr. Pollack?

[silence]

Dr. Evan Pollack

Oh, there it goes. Sorry. I had a little trouble unmuting myself. Well, thank you for the opportunity to just speak on this subject. I'm an internist, and I also oversee a payment integrity program. And we're very, very familiar with this type of testing. And in going through the bibliography that you provided, there's no question that this is a valuable piece of technology that we have at our disposal. Our issues with it is that it's being abused. And we see patients that are going in to get a COVID test and walking out with 25 pathogens that are being-- respiratory pathogens. And I'm not sure that any of them even know that they got this tested. And we see patients that are going into clinics that claim they're specializing in bowel health, and they're having multiple, multiple pathogens run on the GI tract - many of these pathogens aren't even indigenous to this country - and patients that are going in for well-woman examinations and having large urinary genital panels run as part of a routine examination. And in my mind, this is where the problem lies. Hospital protocols, sick patients, that's not an abuse of this. That's where it's probably best used. But those others, that is a problem because these are very, very expensive panels.

Dr. Patrick Mann

Thank you, Dr. Pollack. So we'll take two more, and we'll go quickly through. And then we'll get to our next question. Dr. Regan?

Dr. Terrence Regan

Yeah. I'd like to follow on the last respondent. We do not believe these should be reflexive. They're diagnostic. As part of a quality committee for a large urologic group, we have strict protocols on when these should be ordered that are put out to all our members. And those come from other large urology groups as well. So we do have pretty strict protocols. We do not think that this test should be for a routine or initial UTI. These are for complex patients who are managed by either urologic specialists or infectious disease specialists and should be following pretty strict protocols about who should receive them [inaudible]. I see chronic prostatitis, recurrent UTIs, etc. We're happy to send that into writing, what we think are the good protocols.

Dr. Patrick Mann

That would be excellent. Thank you very much. And then finally, Dr. Block, before we move to question two.

[silence]

Doctor? There we go.

Dr. Mark Block

First, thanks for allowing me the opportunity to participate. In the favor of time, I'll talk fast and keep it very brief. To answer two of the bullet points here, as far as my main hospital that I'm staff at, the outpatient, to the best of my knowledge, has no protocol, i.e., limitation, regarding PCR testing. On the same token, to the best of my knowledge, in the wound care center, where I see a number of patients, it's infrequently used. And to the original question, I could see it being appropriate to utilize this test under limited circumstances where a patient is going through traditional laboratory testing for a bacterial infection, for example, or viral, and they're not responding to the treatments that are being utilized based upon that information, then taking it to the next level and performing a PCR test to try to obtain additional information to assist the patient in their condition. But again, I think it would be on a very limited basis. That's all I have to say right now. Thank you.

Dr. Patrick Mann

Thank you, Dr. Block. Okay. Let's move to slide two. So this second question is discussing what is the appropriate size for a molecular infectious disease panel. And some kind of sub-questions to frame this overall question include: does the recommended size change upon the immune status of the patient? Does the medically reasonable and necessary content of a panel change based on the clinical indications as well as on the geography? Is it reasonable and necessary to test for rare organisms in the outpatient setting? If that's so, why? And we ask that you please provide some examples. Are there customizable infectious disease panels available? Sorry. Why are many testing panels so broad in scope when differential diagnoses are often narrow when based on a thorough clinical history? And then, finally, for infectious disease testing already addressed by current LCDs, namely our respiratory and gastrointestinal panel LCD policies, are the panel size limits appropriate? If not, is there supportive peer-reviewed literature not represented in those LCDs as they currently stand? And we will start with Dr. Benavides. Again, I think I'm butchering your name, and I apologize profusely. So if you could please introduce yourself so I could pronounce your name properly in the future, I'd be appreciative.

Dr. Raul Benavides

No problem. Actually, it's a common thing. Most people call me Dr. B, but it's actually Benavides. So don't feel too bad. But I'm a pathologist practicing in and out of Dallas, Texas. I think, number one, the appropriate size depending upon the mean status. So generally, many of these panels are addressing the most common diseases. Even if you're immunocompromised, you still have vulnerability to those diseases. And as you expand your panel, the rarer ones that would be included in the immunocompromised patients, their pre-test probability on all of those become lower and lower and lower unless you match a clinical characteristic. So you're almost begging for false positives if you get this mega-sized panel. So I think there is a reasonable limitation and a reasonable start to many of these panels. They're meant to screen on a syndromic basis. So really, the strength of the panels is not to test for every disease known to man. It's to differentiate among-- you have a clinical syndrome, and there's a certain pattern, and it can be pretty broad in the respiratory aspect. But you're trying to differentiate among those. And then once you're past those, many times, you have to look at the patient and order two or three specific things. So I think the one or two panels that you see are usually appropriate.

As far are there customizable panels, yes, they do exist. VERIGENE has a respiratory flex panel that allows you to test in one tranche. And then if that's negative, it'll expand out because it was addressing some of these problems. And some of them don't, but that is available. And as far as the testing already addressed by current LCDs, I think since they cover the usual 18-to-22 analyte-wide multiplex panels, especially in the respiratory area, I think that's when I've seen those usually look appropriate. Just knowing that for viral testing, PCR is it. I mean, you can do viral culture, but it'll take forever, and it's very inconsistent. And for some of the-- for some, like the typical bacteria, like chlamydia, pneumonia, and mycoplasma, you want to do PCR culture. It's just not very good. So that's why I think many of these are appropriate. And just to kind of back on the last question, I agree with Dr. Vazquez. A lot of times, some of these, especially in the bronch suite, since you're going there and our pulmonary colleagues are going in there and they get one chance to get that sample, they put in the lower respiratory panel because they're there and they order it. And I don't think that's really our overutilization problem, to the point someone else made. I think it's really on these little labs or clinics that are ordering, to your point, on the first go a GI panel. Or you're looking for COVID, but then you order an entire panel at 800 bucks. That's where I really think the inappropriate use is probably the worst.

Dr. Patrick Mann

Thank you for the very comprehensive and thorough discussion. Let's move on to Dr. Kapoor.

Dr. Hema Kapoor

Hi. Thank you. And I'm going to make comments. And I totally, 100% agree to all what my pathologist colleague just mentioned, everything. A few additional, then, comments I want to make starts with what you have on the first sub-bullet list. Immune status is the key point here, whether we are talking of respiratory infections or GI, because this is the patient populations who are definitely at a higher risk. And also, leveraging the discussion we had on the question number one, that these are the patients who, during the outpatient setting, are at a higher risk with infections, with even opportunistic pathogens. And that's where the value of these panels is: to make a diagnosis. And another point is regarding the geography in rural areas where you may not have specialists available, but then you have immunocompromised patients. And most of the patients older than 65 and with underlying diseases like COPD can have community-acquired pneumonia.

And we know that, in such patients, mycoplasma or chlamydia or other organisms which are outside, like flu A/B, RSV, which are not in the season, out of the season can present a problem in those cases. And the only panels where we have availability of such organisms, which are difficult to grow in the laboratory, are the respiratory panels, which are available. And they range anywhere between 14 to 22 targets. And those are pretty reasonable because larger studies done by CDC also showed, even in the outpatient setting, in adults, you can have organisms which are outside flu A/B, RSV, or strep pneumo. So that's where it brings value. And then touching on the last bullet, customizable, I think that's a key point. Definitely, one size doesn't fit all populations. So having a variety or availability of kind of more than one size of the panels can help clinicians pick and choose based on the clinical presentation of the patient could be one approach which may be helpful.

Dr. Patrick Mann

Thank you very much. And again, if I'm mispronouncing anyone's name, including yours, Dr. Kapoor, please, let me know so I may pronounce it correctly. What I'm hearing so far—

Dr. Hema Kapoor

You were spot on. Thank you.

Dr. Patrick Mann

Oh, it is? Oh, good. Thank you very much. To quickly summarize where we are at right now, what I'm hearing is, additionally to what the questions are showing, seasonality plays a role as well as where the specimen is being obtained. For example, when they're going in for a sample through a bronchoscopy, for example, that those two play a role in what test is selected, in addition to whether or not specialty services are available in the portion of the country where the patient resides. So I'll move on to Dr. Regan, and we'll carry on through.

Dr. Terrence Regan

All right, thank you. Well, complex urinary tract infections, by definition, are kind of beyond the simple syndromic diagnosis. And you're not looking for your typical E. coli UTI. That can be managed by a straightforward urinary culture. We're looking at the complex cases. And for that reason, you're looking for the rarities. And so that's why the panel needs to be broader than just four or five probes. And the other issue is that some pathogens just don't plate out very well on cultures: urea plasma, mycoplasma, aero coccus, and others. And those are the people that urologists and ID people are going to see as an outpatient. And so having a broad panel to pick up these rarities is going to be important for the patients with not the simple, but the complex urinary tract infections. Thanks.

Dr. Patrick Mann

And just to clarify before we let you go: is there a particular size, currently, or sizes, if there is multiple circumstances, that you believe would be medically reasonable and necessary for these complex UTIs?

Dr. Terrence Regan

Right. Yeah. So we have some data that's not published yet that we're going to include in our written-- what we think is appropriate. It has to be broad enough to be able to cover a lot of these because it's just not like 20 organisms or different species of these organisms that cause symptomatic UTIs that, again, may not be as easy to culture. So we'll send that along, but it's going to be-- and that's a good question, but it can range from-- depending on how far you want to dig into the weeds, but you're going to go from 20 to 30 potential pathogens. And we've got some data to show how you can pick these up, the more pathogens you test for. And we're going to send that along to you.

Dr. Patrick Mann

Great. Thank you very much. Moving on to Dr. Jackson.

Dr. F. Wilson Jackson

Yeah, hi. Thanks. Just to kind of talk to the fourth bullet point down regarding the customizable infectious disease panels, I don't know if there's anyone from the industry on this panel or whether you've spoke with them already, but these are kits. These are manufactured kits. And perhaps a solution to reduce the cost and over-testing, particularly for the inappropriate organisms screening in the clinical scenario, would be to ask the industry to say, one, "What's your economics behind creating these kits? Why do you have a panel of 30 versus 20 versus 10?" And the economics might be-- there might be a compelling reason why they do it that way. But it leads to another question for the industry, as perhaps they can create kind of scenario-specific-- these kits. These are cartridges that you just plug into the machine like a blood sample. So for example, within the GI, which is my area, could you have a geographic kind of kit for-- a cartridge, so to speak. In other words, if you're in the northeast versus in the southwest, could you have a traveler diarrhea kit, which would narrow the focus? Could you have immunocompromised kits for someone who's immunocompromised post-organ transplant? So I just encourage to engage, if you haven't already, the industry regarding kind of their economics behind creating these kits. And we want to keep it narrowed focus. But I think you're exactly right. Oftentimes, we have a great narrow clinical differential, but then we get a panel of 10 tests back, 1 of which may be irrelevant to the-- or test positive and help us.

Dr. Patrick Mann

Great. Thank you very much, Dr. Jackson. Moving on to Dr. Block.

Dr. Mark Block

Yeah. I'll try to be brief again. One of the things that comes to mind, the concerns that I have, is some standardization as far as some of these panels. It would probably be helpful if there were some type of stringent parameters in place, if possible, to dictate that. I could see, in some cases, where too few analyses are not helpful at all, whereas too many are very costly. So to kind of bring that in alignment, again, I go back to what I initially said. I think there needs to be some kind of standardization of parameters. Also, question whether it's clinician driven versus lab driven. I think there has to be some kind of balance there. And the last statement I wanted to make is that there's an LCD-- trying to look for the number here; I lost it. But it looks like this LCD, which deals with these particular issues - I think it's L39038 - seemed to do a lot of the heavy lifting. I can't speak to the GI/GU or other areas out of my area of expertise. But from what I read through this, I think there's a lot of helpful information. And it's, again, a great starting point for crafting some additional policy. That's all I have to say. Thank you.

Dr. Patrick Mann

Thank you very much, Dr. Block. We'll do Dr. Kapoor, and then we'll move on to the next question. And before I let you speak, Dr. Kapoor, one other thing to consider while we're having this discussion is also whether or not there needs to be different standards around whether or not these are qualitative or quantitative tests. So in other words, do the answers change if it is a present or not present versus a quantification of how much is present through the testing? Please, go ahead, Dr. Kapoor.

Dr. Hema Kapoor

So I just wanted to follow up on Dr. Block's comment. I totally agree that we really need to keep the abuse addressed here. But based on our discussions, there is special populations, specifically immunocompromised, where we do need more than five targets. The current policy is written for the respiratory pathogens up to only less than six or up to five targets. And I think one we have seen in the laboratory that helps us-- because we don't get the clinical information on the patients. So being in the reference lab space, another way to address or suggestion is to have specific ICD-10 codes listed on the policy. That way, it is kind of-- that gives an educational piece to the providers to use these panels in the right scenarios, which are clinically indicated and help the laboratory as well to keep that in the focus.

Dr. Patrick Mann

Thank you very much. So a couple of things to mention before we move on to the next question. If the panelists feel comfortable and would be willing to, we would love to have any input you can have towards both the size of panels you think would be appropriate, even listing what organisms you would consider to be critical or different scenarios. So I understand that that is probably an easier modality to address the question more thoroughly. And for those of our panelists that are willing to provide that, we'd be grateful. Moving on to our next question. Next slide. When developing molecular testing guidelines, would there be a one-size-fits-all set of rules, and if not, what subgroups are required? For example, groups like organ system, e.g., respiratory or GI tract, or groups like disease category, like pneumonia and sinusitis. As a subset of questions to this overall topic, we are aware that due to the difficulties in culturing viruses, as was mentioned earlier by one of our panelists, molecular testing for viruses is a superior means of testing patients. Is molecular testing for other categories of infectious organisms, for example, bacteria, fungi, and parasites, superior, and if so, superior in which clinical circumstances? And finally, is there any peer-reviewed literature to support the superiority of testing in these clinical circumstances?

[silence]

Dr. Kapoor?

Dr. Hema Kapoor

So for your [trending?] question, I think it should be by, as you said, the syndromic approach based on the organ systems. And then within that organ system, there could be a scope for creating subcategories by the disease, like pneumonia or upper respiratory tract infections, so that that can make it-- or same as we heard in the UTI, to really complicated UTI or a complex UTI. And then the same is with the gastrointestinal because gastrointestinal can be the chronic diarrhea, which is there for seven days. But then if you are looking in really immunocompromised patients, there could be an oblique situation. So that's what I would like to mention in this question. For the sub-bullet, there is evidence that the molecular methods have definitely increasing capabilities for detection, specifically organisms, even in the bacterial space, which are fastidious or slow growing because if you take, for example, a mycoplasma, it can take 14 days to grow.

Yeah, and some of the fungi which can cause bloodstream infections. And Candida Auris is a simple example where you want to keep the patients not entering the hospital with those colonized-- or with those infections. Parasites, I would say, depends on-- again, the only way we offer parasitic testing at the moment is by direct ova and parasite. The sensitivity of those methods is much lower than the molecular. So if you're talking of, say, immunocompromised patients, HIV or others, where there could be parasitic infections which can lead to the more extensive infections, in those cases, there is value. But otherwise, for routine testing, for stool ova/parasite in immunocompetent patients, you probably don't need the molecular testing. But there is value in those circumstances, like difficult-to-grow organisms. TB is one example, which takes an awfully long time to grow. So to make treatment decisions early and also keeping the patients out of isolation, those are some of the situations where these molecular panels definitely are more helpful.

Dr. Patrick Mann

Great. Thank you very much. Dr. Jackson?

Dr. F. Wilson Jackson

Thanks. I'll just follow up on the GI-specific component of the question. I mean, we all know that the logistics of processing the stool specimen in the traditional manner, culture and O&P, is fraught with all sorts of just logistical challenges in the clinical environment. That's where I live the vast majority of my work life, is in the office setting. You order a stool sample, again, in the traditional manner. The patient is given a plastic cup, told to go home, collect a sample. Depending on the time of day, it may sit in the refrigerator or, who knows, on their countertop overnight. They bring it in. They drop a kid off, do some errand along the way. And it sits in the front seat of the car, and it's 98 degrees outside. It gets dropped off at the office. It then gets picked up by a reference lab. You know the scenario here: it's just fraught with all sorts of places during which the quality of the specimen gets degraded, and the quality of the test result gets put into question. The PCR bypasses all of that because I don't think there's much question on the superiority, at least from a GI component, in terms of the diagnostic accuracy. And the reference, I admittedly didn't read everything throughout the 70, 80, 100 references here. But reference number five I think speaks to the last question in the bullet point there regarding kind of the value of this test, particularly from an economic perspective. I mean, that particular article said there was almost $300 savings in terms of unnecessary testing amongst GI pathogens.

Dr. Patrick Mann

And just for the record, you're talking about the gastrointestinal PCR panel, improved [crosstalk]?

Dr. F. Wilson Jackson

Yeah, yeah, GI specific. Yeah, GI specific. Yeah.

Dr. Patrick Mann

By [inaudible]. Yeah. 2018. Okay. Thank you. Dr. Regan?

Dr. Terrence Regan

Yeah, I just want to-- I agree with Dr. Kapoor that it really has to be divided up by, I think, organ system. And then that can be broken down, like in urinary tract, between chronic urinary tract infections and sexually transmitted diseases because they may have a little different panels. And just briefly, in terms of the size of the panels, not to go back to question two, but it makes more sense to have a wider panel if you're looking for rarities than having a smaller panel and then having to have three or four tests till you find the organism. So economically, it may make more sense to have a larger panel. And that's the end of my comments for question three.

Dr. Patrick Mann

Thank you. Thank you, Dr. Regan. Actually, if we can unmute you again, I do have a question along those lines. So to what extent can we rely, though, on a very thorough clinical history and other elements of that to narrow down the differential for these circumstances?

Dr. Terrence Regan

Yeah. It can be difficult, right, because, again, we're not talking about your typical urinary tract infection. And I mean, I think that's the big issue here. We're not recommending that for that scenario. These are really the complex cases. In terms of the history and physical, that may help you narrow it down somewhat. But most of these patients tend to be very, very complex and, oftentimes, have gone on for a number cycles of different antibiotics. And really, drilling down to find out the exact organism or the multi-organisms that are causing the syndrome is important. So it may be helpful somewhat, but I don't know right off the top of my head whether a good history and physical and other information there is going to actually help you drill down that panel any narrower. But if we can find some information on that, that'd be great. But at the present time, I don't have that for you.

Dr. Patrick Mann

Thank you very much. If you do come across something that would be helpful, especially in the peer-reviewed literature, that would be excellent. It would be appreciated if you could send that to us.

Dr. Terrence Regan

Oh, that'd be great.

Dr. Patrick Mann

Thank you. Dr. Vazquez?

Dr. Alfredo Vazquez-Sandoval

Yeah, hello. A couple of comments. I agree with Dr. Kapoor regarding tuberculosis PCR. Mycobacteria PCR, I mean. It can take a long time to grow. And the implications for public health make it a must when you're trying to throw that out and to prevent exposure. Regarding bacterial pneumonia, the literature does support these tests being more sensitive. But at the same time, when you have a really sensitive test, a lot of these plates are going to be colonized. And I think that's one of the questions. To my knowledge, the only results around patient center outcomes that I could find-- and it was not on the list that you guys provided, and I can provide the reference later. Basically, it was the Flagship II study, which was published in Lancet Respiratory last month, actually. Basically, it was looking at patients with pneumonias and gram-negative pneumonias-- sorry, risk factors for gram-negative pneumonias. And in those patients, it did decrease the exposure to antibiotics by close to two days. So it has a really good selection criteria and such, so I'm happy to provide that reference.

Dr. Patrick Mann

Thank you very much. That's great to hear. Dr. B? And I apologize in advance for the squeaking sounds in the background. I do have a husky that is enjoying her toy during our discussion.

Dr. Raul Benavides

Well, I'm glad she's having a good time, too. Number one, just kind of going down, I do agree that you can have different panels depending upon the circumstances. Clearly, some of my colleagues have outlined the need, even by complicated versus non-complicated UTI. You have a complicated UTI, you're going to have a set of bacteria and all those that just come along with it, and you see it. And you put those into the, quote-unquote, "syndrome" that you're looking for, and that's the right size. I think what also comes into how big these panels are, sometimes you use an instrument and using the same instrument for several panels, and you have a certain amount of slots you can fill with primers and certain channels. And if you have the extra channel, sometimes the vendors just say, "Well, let's add this because it's there." In the same point that whenever BioFire added coronavirus, they flipped out another test for that one. So I think that's why sometimes you see bigger panels that are just added. I think they're just [building it?].

I think another thing that we have to take-- that's a difficult subject to really get good data on is-- even if there are clearly things that are superior that we've gone through, where it's clearly superior if you put them head to head, the molecular is better. But even if it was the same, the timing is a big aspect because if you can get someone on targeted therapy, that saves you hospital days, that saves you extra tests, that saves your patient, and it's the global healthcare that you're looking at. If you're doing it right, it's cheaper to test more people and avoid an X number of sicker patients if you can treat them early. So that's just a really hard macroeconomic number to come by because I've seen some papers that show clear economic advantages and others where length of stay never really budged using some of these large panels. But that's the idea. It's really the speed. That's why the ME panel that's put out by one of the vendors is a clear winner. I mean, even if you could-- I mean, one of their tests has a flaw. The crypto channel is not very good. But still, in general, you get most of them ruled in or out within an hour of them landing in your facility. So I think the speed also comes into light, as has been addressed by some of my other colleagues.

Dr. Patrick Mann

Thank you very much, Dr. B. Moving on to Dr. Block.

Dr. Mark Block

Yeah. Doing my research for this, I came across some reference to an article. And I'm going to just read the two brief lines which I think can express it better than I can. Cuchi-Burgos evaluated the clinical utility of incorporating the clinical laboratory workflow of commercial real-time PCR for dermatophytes detection in nails. And in the end, what they concluded, that although the sensitivity of PCR compared to culture is 92.8% and time of response decreases from days to hours, PCR testing is not proven to be better than the standard of care with direct microscopy and culture mediums. So let me take that to the next level as well: so when a clinical environment test is done, basically, in my geographical area, the standard care for oral is terbinafine.

Studies have shown, I believe, that terbinafine now is maybe 70% effective. So if the terbinafine is not effective, where do you go from here? I don't think there are many options open. So number one, one has to ask the question, "Why would you do the PCR testing as a first line?" First, I would argue that it shouldn't be a first line of testing, number one. I could see it being done if, for some reason, the patient is immunocompromised, and for some reason, the patient has to go on oral Lamisil, terbinafine. And there may be some health issues, but you want to make a decision if you're going to want to give this medication. If the risk-reward is there before you even put them on it, then I could see maybe doing the PCR testing. But I think that would be a very limited set of circumstances. So just wanted to share that, and that's all I have to comment on right now. Thank you.

Dr. Patrick Mann

Thank you very much, Dr. Block. Before we move on to Dr. Kapoor, I do want to ask-- there are some people that are in our CAC groups that we haven't heard from yet. And we understand if you don't have any comments for each and every question, but we would love to hear from as many of the CAC members as possible. Valuing all the input from various different sources. Dr. Kapoor, we'll hear from you, and then we'll move on to our next question.

Dr. Hema Kapoor

Just one additional comment to piggyback on the comment which was made on the speed. Just wanted to talk from the perspective of microbiology lab from where I come, is that the specimen types-- for example, upper respiratory tract or respiratory tract, per se, like spiro, or nasopharyngeal or throat swabs or even stool, these are all the matrices which already harbor so much of normal flora and junk that even in the best hands of microbiology culture methods, it's not easy to isolate the pathogens from them because you have to go through the enrichment procedures and then use the selective media to grow. And the more fastidious the organism is, the longer it takes for them to grow. So keeping all that in mind, that's why molecular methods are definitely more specific as well as sensitive when we talk especially on those special circumstances. And again, I would say keeping the patient first who are more immunocompromised and have the risk of these serious infections where time is essence.

Dr. Patrick Mann

Thank you very much, Dr. Kapoor. And that actually provides us with a great segue into our next question, so I'll go to the next slide. I would ask the panelists to discuss how the detection of dead organisms impacts the usefulness of the molecular test results, which includes a discussion then, as was brought up earlier, about colonization and quantitative versus qualitative PCR. But at least addressing at first the detection of dead organisms. Dr. Pollack?

Dr. Evan Pollack

Yeah, thanks. So [laughter] here's my comment on this. And I think it goes back to what I had said previously. So in the right hands, in the hands of a specialist, looking for something specific with a patient that is presenting with a clinical scenario that's making one suspicious of a particular organism, then in that case, this testing is going to be great. But the problem is if you're just using it in a shotgun approach and sending everybody for the same testing no matter what, then you are going to get dead organisms and clinically insignificant results, which may make it difficult to treat the patient, so. And listening to what people have said - and there's a lot of very bright specialists here - in the right hands, this is a great thing to have. It's a great tool. The problem, and I guess the challenge and why we're all meeting, is making sure it is done properly and in the right clinical scenario.

Dr. Patrick Mann

Thank you very much, Dr. Pollack. And I think that one of the questions that we would want to know and kind of follow up to that would be how best to determine the prerequisite conditions that would lead to the molecular tests. This is almost kind of going backwards to ask the same question as question number one, which was, what are the steps of clinical decision-making that lead to ordering a molecular infectious disease panel? Especially given that, as was said in this meeting, there are circumstances where the molecular test is not the first-line test in the process of evaluating a patient and trying to determine in which circumstances it would be medically reasonable and necessary versus in circumstances that there has to be other steps for you to move on to a molecular panel test. Dr. Kapoor?

Dr. Hema Kapoor

So I think the best approach to use these panels is testing to establish a diagnosis and then for the management of the patient illness. I think one way for this approach to not have the dead organisms come in the way of making a diagnosis is these tests should not be utilized for test of cure. That's the recommendation, from a microbiology standpoint, we make, always. And we saw that in the COVID-19 when the earlier recommendations were to see, "Can you clear the SARS-CoV-2?" And for a long time, people could not, and we were picking up the dead organisms. So I think staying away from offering a recommendation that-- no need to use these panels for test of the cure, that post-treatment have no value. That's the one way we would-- I mean, I would like to make that comment.

Dr. Patrick Mann

Thank you very much. Dr. Regan?

Dr. Terrence Regan

I was going to say something that's similar to what Dr. Kapoor had to say, that it's not tested for cure. And I can't speak for the GI or the pulmonary or some of the other indications, but these are not going to be used in urology for asymptomatic patients. So these are patients who are symptomatic. And you have to also have good lab technique, etc., to make sure that there's not contamination, which can happen with regular cultures and alike. But a lot of it comes down to clinical judgment as to what you're seeing in the results and the patient's symptoms, etc., and how you account for those. So if somebody had tested positive Corynebacterium, which would be unlikely to cause a symptomatic UTI, you certainly wouldn't treat that if you thought that was a dead organism. But again, there's some clinical judgment there, and using it appropriately has been mentioned many times. These are not for screening tests. And I think urology does not feel that these PCR tests should be done for screening. These are for complex cases, and so asymptomatic patients. And I think that's going to really kind of weed out concern about treating dead organisms, so. Thanks.

Dr. Patrick Mann

Thank you very much. Just before we move on to the next question, is there any comments from the GI or respiratory experts we have on our panel to address what Dr. Regan just brought up? Dr. Jackson?

Dr. F. Wilson Jackson

Yeah, I'll just echo that. I mean, a lot of this is just clinical judgment. It's like what we do every day: you order a test; you get a result; you interpret it and apply it to the clinical scenario. So yes, there could be some false positive dead organism. But there's a little judgment that comes into play there that, hopefully, will be properly applied.

Dr. Patrick Mann

Thank you, Dr. Jackson. Okay. Let's move on to our next question, question number five. So this is looking to the future. We know that the molecular field's exciting, with a lot of new directions and a lot of new possibilities for greatly improving patient care. So considering the multitude of new directions for infectious disease testing, we have this series of questions. First, what are the physical circumstances, if any, where molecular testing is appropriate as a primary diagnostic test? What are the panelists' thoughts on pooled organism resistance testing, which, as I currently understand it-- and I am open to having it further defined, but as I understand it, it is testing a group of organisms all at once to see if any of them become positive, which would make the test, as a whole, positive. Next question. What are the panelists' thoughts on microbiome testing, such as gut microbiome testing? Next question. Are there any indications where standard microbiology lab work, for example, culture plates/broths, biochemical organism identification, is necessary and molecular testing is not? And then, finally, what evidentiary standards would you require to consider a test no longer investigational but rather appropriate in the clinical setting? For instance, at what point would a new molecular technique be considered safe and effective for patient care, and how would you determine this? Dr. Jackson?

Dr. F. Wilson Jackson

Again, the microbiome is a super exciting area, and I think it has great promise. But our current opinion on this within the GI standards is it still should not be used outside of kind of a clinical trial environment. There's just too many unknowns right now, so. Unfortunately, the stool testing for the microbiome has kind of bled into the commercial arena, and patients come to me with these three-page kind of documents of their stool analysis by some reference lab somewhere that they paid out of their own pocket for. This data is really uninterpretable right now, so I think that we should be very cautious around microbiome testing or endorsing that in terms of an LCD at this point in time.

Dr. Patrick Mann

Thank you. Just to follow up on that, what would you require to start accepting that new molecular technique? What kind of things would you be looking for to move you from the investigational and exciting to the routine and clinical?

Dr. F. Wilson Jackson

Yeah, I think we need some kind of well-constructed clinical trials. But I think you do an intervention, and you assess the response on the stool study. So for example, there's a lot of interest in the microbiome as it pertains to obesity. And can you manipulate the microbiome to impact kind of the metabolic syndrome? And perhaps there's going to be some studies that'll come out where you can have some objective measures of the metabolic syndrome in addition to just pure weight. And then you look at the microbiome and are you making a meaningful change there. But there's so much complexity in the microbiome, and there's so much variation from person to person. There's so much that plays into it that I think we just be cautious right now in applying or interpreting this data, so. And obesity is just one of a whole series of things. Within my own practice, I see a lot of inflammatory bowel disease and a great deal of interest in how can we manipulate the microbiome in inflammatory bowel disease in order to improve long-term disease maintenance. Again, the jury is still out on these things, and there's a lot of interest. But right now, I think it's premature to kind of cover these things at this point.

Dr. Patrick Mann

Thank you very much. Dr. Kapoor?

Dr. Hema Kapoor

So for the resistance testing in the bacteria, I see value in a few circumstances, like in the H. pylori clarithromycin resistance testing because it's hard for us to grow the H. pylori and give a sensitivity testing. So having a molecular assay for such examples or in gram-negative bacteria because we are seeing a more carbapenem-resistant picture because carbapenems are the last resorts of antibiotics available to us. So in special circumstances, you can have these kind of scenarios where there is value, but I would say not for the pooled organism resistance testing. It's also in more research setting at the moment, but not ready for the prime time to bring it for the clinical utility. I totally agree with the comments on the microbiome. We feel the same. It's still not ready for the prime time.

So for the last but one bullet, standard micro testing, as you've mentioned earlier, too, for routine UTIs where we expect E. coli to be the 80% cause of organism, it can grow pretty quickly in the lab. Now, with the automation and with rapid susceptibility testing, easily, a result can be turned back within 36 hours or 24 to 36 hours. So that's where it still holds good. And same for routine wound cultures where you're going to grow Staph aureus. So typical microbiology is still expected to be there and offered there for more years to come. And I think that the last bullet is when there is enough evidence for analytical and clinical utility of a new technology, I think that it should be made available to the providers rather than waiting too long for guidelines to be implemented. So maybe good studies or showing the evidence can be a good step to make new molecular techniques available for the beneficiaries.

Dr. Patrick Mann

Thank you very much. Moving on to Dr. Kwong.

[silence]

Dr. Jeffrey Kwong

Hi. Hello. Can you hear me? Yes. Okay.

Dr. Patrick Mann

Yeah, we can hear you.

Dr. Jeffrey Kwong

Sorry. Sorry about that. Thank you. So Jeff Kwong. Thank you for allowing me to participate. Just, I guess, for the first question about clinical circumstances and molecular testing as a primary diagnostic test. And I think that would be based on the condition or the disease or the symptomatology that's there and also just in terms of the greater impact or the ramifications of the potential diagnosis that you're searching for. So if it's a potential public health concern, such as COVID or influenza, and you need a rapid primary diagnostic test, obviously, that would be first line. I do a lot of STI work. And so in that situation, I think that's important from a public health standpoint as a primary diagnostic tool and also, from just a patient comfort level and patient-centered approach. I know this was talked about earlier, just even with regards to stool sample collection, etc. For STI testing, for example, I can do a single swab and get multiple potential pathogens identified versus doing multiple swabs and multiple smears, etc. So I think from a patient-centered standpoint, it is the way to go to make quality of care better for patients, so. All I'll say. Thank you.

Dr. Patrick Mann

Thank you very much. That's very helpful. And thank you again for speaking up and providing a new perspective. It's great hearing from you. So I think what we'll do now is we'll move on to question number six. And following question six, we will additionally see if there's any other comments for the previous questions and then discuss the next steps from there. Thank you very much. So for question number six, currently, there's a paucity of established clinical guidelines and decision trees addressing proper use of molecular infectious disease testing, as can be seen from the 100 references that we have provided and what's found within the references. What is the current progress among experts in the field towards creating more comprehensive guidelines? And as a background, per reasonable and necessary language in the CMS internet-only manual publication 100-08, Chapter 13, Section 13.5.4 and based on the 21st Century Cures Act, how long should a MAC wait for published peer-reviewed evidence that meets the above criteria before determining that the evidence is not available and non-covering a test or category of tests?

[silence]

Dr. Jackson?

Dr. F. Wilson Jackson

Yeah, I'll just kind of fill the silent void there. I think we have to look towards the society guidelines. The first reference in your bibliography here pulled out the standards amongst the infectious disease societies. I think we look to the national societies, whether it's infectious disease, pulmonary medicine, gastroenterology, urology. I think that's where these things are really vetted by some true experts in the field and get a consensus. So that's, unfortunately, a long process, and unfortunately, it also is not always timely. But these consensus panels, I think, are a good reference point to guide Medicare policy.

Dr. Patrick Mann

Dr. Block? Thank you, Dr. Jackson.

Dr. Mark Block

Yeah. That's a tough question to answer. Are you looking for a generic statement on all policy or just on this specific policy?

Dr. Patrick Mann

Well, we're mostly focused on this policy. But in general, this is a larger concern as well given that with the 21st Century Cures Act, there is a lot more emphasis on providing policy based on peer-reviewed literature and expert opinions. And in the case of molecular infectious disease testing, finding relevant peer-reviewed literature is not always readily available.

Dr. Mark Block

Is it already published in the IOM, or is it not specifically referenced as far as time?

Dr. Patrick Mann

If I understand your question correctly, you're asking, with the regulations from CMS, is this question answered in any shape or form?

Dr. Mark Block

Correct.

Dr. Patrick Mann

And I think that it's left a little bit more arbitrary. And with this way that the CMS internet-only manual and other regulations are published, a lot of it is left up to the MACs in discretion and determining what evidence is required to come up with these policies. However, there is that element that we have to, when we're writing our policy, not only supply what evidence is being used but also discuss the evidence and how we use it to make the policy, if that helps clarify.

Dr. Mark Block

Yeah, well, as alluded to by the previous speaker, I would agree that-- I think a lot of it would be dependent upon - and since you're reaching out, in most cases, to the assistance of the specialty societies or associations - reaching out to them and looking at the magnitude of the question that's being asked. And the information you're looking to glean rely on what's reasonable in order to do an appropriate evaluation, literature search, etc., to determine what's appropriate. So I know I'm not giving you an exact answer, but I guess it could be six months to a year, in my mind. In something that's very convoluted and in-depth and controversial, I think just a few months is not going to play out very well. So I think there should be some dialogue between both the MACs and the societies that you're asking to assist. I don't know if that helps you with an answer, but that's kind of my answer right now.

Dr. Patrick Mann

Thank you. Dr. Vazquez?

Dr. Alfredo Vazquez-Sandoval

Yes, I agree regarding that. For established diseases, usually, waiting at least for their societies to pronounce a statement seems to be the best route, at least for diagnostic testing. But also, we need to take into account for emerging diseases, like we experienced with COVID and monkeypox. Probably an exception should be done for those specific type of crises.

Dr. Patrick Mann

Dr. Vazquez, just to clarify. Are you saying that coverage should not be provided until a society weighs in on it? I just—

Dr. Alfredo Vazquez-Sandoval

It depends—

Dr. Patrick Mann

--want to make sure I understand.

Dr. Alfredo Vazquez-Sandoval

It depends on the setting. The societies order randomized controlled trials. Well, in testing, it's going to be difficult to get randomized controlled trials, but I guess evidence that shows a difference in patient-centered outcomes-- because we have the experience of procalcitonin, right, for pneumonias, which is a good test, but studies have shown that don't make a difference because clinicians don't follow it, right? So I think that a good period of waiting till evidence is published about this making a difference in patients' outcomes is important, with the exception of emerging diseases. When we have a crisis like a pandemic of highly infectious organisms like COVID or monkeypox, then it's a different situation.

Dr. Patrick Mann

Thank you very much. Moving on to Dr. Kapoor.

Dr. Hema Kapoor

I agree. It is a difficult question to answer. And definitely, this is the gap. And we also observed-- I mean, as my previous colleagues have mentioned, it takes a long time. But would the analytical and clinical validity be considered as evidence? And then once that is established, then the Medicare beneficiaries should have the access to this molecular testing? Because that will determine that that's going to be helping them for the best treatment in those circumstances.

Dr. Patrick Mann

I mean, I think that that's part of the discussion we wanted to have here, was what level of evidence is appropriate for considering a test medically reasonable and necessary per what Medicare has in the statement and the regulations, the Social Security Act baseline? And so kind of the question is that when we have a test-- and there's initial small papers out. But at what point does the test move from, as a previous question said, investigational to accepted in the larger field, as well as accepted by the people that represent the field as experts? And where's the threshold at which we can cross over from something that's investigational and exciting to routine and clinical? And who holds the reins to that level of evidence as well? I think that's the essence of what we're getting at. We're looking for clinical utility and clinical validity, as shown by the literature or the guidelines provided by the societies.

[silence]

Moving on to Dr. Regan.

Dr. Terrence Regan

Yeah. It's an interesting question and a tough one because when you have a disruptive technology like this, it can move through the community much faster than the guidelines can keep up with. It makes it difficult for the carriers. We're all interested in giving the best care for the beneficiary. And so as it gets more accepted in the community and utilized because it shows clinical validity and results, especially in each of our fields, I think we can probably have all different examples of where it makes a big difference in urology, chronic, complicated UTIs. There is continuing evidence to show that it's superior to regular urine culture. But we're not talking about routine-- we're not talking about routine infections. We're talking about complex infections where the data continues to show that the PCR testing is superior to regular cultures. I think the evidence is already accumulating. But if we wait till society guidelines are published, it tends to be-- it tends to take a while for the guidelines to actually synthesize all the data and for them to come out and have them published. By that time, much of the community is already using it. I'm a little bit concerned there'll be delay for the beneficiary on a disruptive test that's already starting to show clinical validity across a number of different specialties. And I think it's important. We're not talking about reflexive testing. We're not talking about routine testing. We're talking about these complex situations where there continues to be data to show it's superior to regular cultures.

Dr. Patrick Mann

Yeah, and I think that part of the question there is-- there's obviously an inclination to go towards anecdotal kind of findings. So you do have cases where a new test saves the day, but obviously, anecdotal is not to the level of evidence - I think we'd all agree - needed to get a test into the realm of clinical utility and clinical validity. However, as you were saying, waiting for the consensus of an expert society is not always fast enough for breakthrough technology. And so that's what we're kind of asking here, is, "So where do we look in between those two extremes to find evidence that we are adequately covering, in a timely fashion, technology that is needed to improve the Medicare beneficiary care without too quickly adopting coverage for something that has not been thoroughly tested and vetted by the experts and the people in the field using it?" Dr. Pollack, would you like to speak up next? We already just talked to Dr. Regan, correct?

Dr. Evan Pollack

Yeah, sure. And probably just reiterating a lot of what's been said, but certainly, done in the right hands, these tests are extremely valuable. And so complex patients seeing specialists, or there certainly may be a reason in a country where some of the specialties aren't available. But certainly, seeing a physician who is concerned about a more complex disease, that's where these tests are for. The problem and, I guess, why we're all here is how do we make sure that those tests are ordered by the right people? And what would it take to make sure that they're not being just done haphazardly by entities that shouldn't even be ordering it at all? And being in the payment integrity arena, I could go on with stories about some of these panels that we've seen ordered routinely over and over again on the same patients, weekly or sometimes twice a week, where it's clearly being abused. And so what level of either diagnoses or prior treatments is necessary to really justify the use of this type of technology?

Dr. Patrick Mann

Precisely. And as one of my CMD colleagues has said in the background, what we're seeking to do is to cover something that is at least as good, if not better, than the available alternative, but not exceeding what the patients need. Thank you very much, Dr. Pollack, for your comments. Dr. B?

Dr. Raul Benavides

I think in the intervening time, a lot of people have said kind of what I was alluding to. I mean, just on the time. It takes time from when something's FDA approved to even get it deployed in a lab and then to educate people, and then they get to use. And then the physicians get to evaluate whether or not they think it's worth ordering. And then, once they start ordering in volume, you can start publishing. And then you finally get things out. Then you have to-- once you have a critical mass of publications, then you can decide. And then that's when you theoretically want to determine it, but there's a gap between that time and when guidelines will be adopted because it just takes a long time for that to be put in. I mean, you could go by volume because, generally, once a test is introduced, even if the vendors think it's great, I've seen physicians just say, "This just isn't worth it." And the volumes, they never take up, and you can kind of tell they'll never take off. But that doesn't allow for massive clinics who are over-ordering a test or two. And so that clouds any judgment. How do you know? How do you determine that? There's a large group of physicians who are over-ordering it other than just outright Medicare fraud. So I think that's where the big gap is between, one, the critical mass of literature and then who's going to review it on your behalf in the intervening time between, when a society guideline comes out.

Dr. Patrick Mann

Thank you very much. Dr. Manaker?

Dr. Scott Manaker

Thank you. Two quick comments, one about guidelines, one about clinical scenarios. I don't think, realistically, you can wait for guidelines. The decision to proceed with a guideline for any given society is complex and dependent not only on the availability of a published evidence base, but other decisions, such as what issues are most pressing, given limited resources of the society and how they choose to pursue guidelines. Similarly, I don't think you can make a decision with an arbitrary amount of evidence base because you may have a half dozen or dozen well-designed studies that demonstrate clinical utility and benefit without much disagreement. But you might have, for a different scenario, 20 studies where there is conflicting evidence, and it remains controversial for a longer period of time. So I don't think you can make the determination based on, necessarily, the quantity of evidence that's been published or the existence of a guideline. I think you're going to have to be making an ongoing decision as you review what follows the 100 articles that you've circulated to us.

The second comment is hearing several of the clinical scenarios presented tonight, I suspect that you can take a look at some of the abusive or near-abusive clinical scenarios for screening or routine use of these tests, as opposed to situations with appropriate clinical circumstances preceding diagnostic testing having returned controversial or non-diagnostic, that you could come up with a policy with some requirements. And it would be very easy for high-volume, potentially abusive providers to receive some record requests to determine are they or are they not ordering these in accord with such a clinically crafted payment policy. So those would be my two comments. Thank you.

Dr. Patrick Mann

Thank you very much. Moving on to the person named Bryan there, which-- we didn't have a last name, but we believe is Dr. Youree. If I am wrong, I apologize.

Dr. Bryan Youree

Yes, this is Bryan Youree, infectious diseases. I was just going to comment - and some of this has already been said - that I suspect you won't see any guidelines from the societies, whether it be Infectious Disease Society of America, to make any formal comments, particularly on outpatient respiratory and urine molecular testing for some time because, just like routine cultures, it comes down to how the specimen is collected and how would you even begin to validate a study like those in a real-world setting. I mean, I routinely get referrals from skilled nursing facilities where they have contracts and they no longer do cultures and are repeatedly testing Foley patients for molecular testing and likewise, sputums that would never pass oropharyngeal contamination of the micro lab with some of these outpatient respiratory. And they come up with multiple different pathogens. And so it's going to be extremely difficult to validate those types of studies. So it's a completely different beast than an inpatient setting where collection is controlled and you know the circumstances as to why these specimens are collected. So there could be widespread abuse of these and, ultimately, overutilization of antibiotics based on tests that are very difficult to validate as they stand right now.

Dr. Patrick Mann

And Dr. Youree, do you have any thoughts as to solutions for some of these very insightful and valid problems that you brought up? Dr. Youree needs to be, I think, unmuted if we haven't already unmuted him.

Dr. Bryan Youree

Yeah, I think that just would have to come from somebody that's far more intelligent than me in terms of how you can rule out contaminated specimens in those scenarios. But again, that still doesn't determine how the specimen is collected and whether there may be compromising factors that would rule the test invalid. It's much easier for emerging pathogens where you-- something that's not common in the community. But for routine bacterial and even some viral processes that could be colonizing the upper airways, that can make it extremely difficult from a molecular standpoint.

Dr. Patrick Mann

And do you have any comments on a frequency scenario - I see you've muted yourself again; I apologize - in terms of the increased frequency of these tests that you've mentioned, coming especially from skilled nursing facilities?

Dr. Bryan Youree

Yeah, I think it just has to come down to set limits on how frequent because, again, testing for cure, we see that with urine cultures to begin with in asymptomatic individuals. Or it's based solely on appearance or odor of urine, which has been clearly shown to have no correlation as to whether someone has an active infection or not. And so there would have to be, I think, probably, some degree of guidelines on the frequency of the testing.

Dr. Patrick Mann

Thank you very much. Moving on to Dr. Vazquez.

[silence]

Dr. Alfredo Vazquez-Sandoval

Yeah, pardon my ignorance. What's the current process? When a new test comes out, how or when does it start being covered?

Dr. Patrick Mann

Well, that's a very complicated question. And part of one of the reasons why we're holding this CAC is to try to help guide us in what would be seen by experts in the field towards what we should be looking for in levels of evidence, where to look for the evidence, and at what point do we meet thresholds where the experts and the people that are using these tests in the field feel that we are doing an adequate job of providing clinically utile and clinically valid testing and protecting the patients from undertested and under-vetted testing.

Dr. Alfredo Vazquez-Sandoval

Yeah, I get it, because I think, right now, in a sense, it doesn't seem that there's a process, that we're trying to establish a process. But I am assuming, right now, these things get approved without any discussions like this, like this group, because I agree with some of the points that my colleagues made regarding guidelines. Yes, they can take sometimes up to 10 years to be re-evaluated, now that I think about it. But a group like this where they can review evidence, I think this should be the way to do it. But the question is - I agree - when to trigger to have a discussion like this, at what point from a new test being developed? What should be the triggers to have a group like this to work on answers? And I don't have an answer for that.

Dr. Patrick Mann

Thank you. Dr. Block?

Dr. Mark Block

Yeah, I just wanted to clarify a statement I made earlier. As a general rule, something like this would be initially covered. And then if it was perceived as being problematic, a draft policy would be formulated, a panel like this would be convened, and we would discuss and try to offer recommendations. So if I'm correct, that being said, I don't see any harm in putting it out to societies to help with literature as has been done in the past and get experts to contribute on a panel. So I don't see it being a hinderance to the patient population during that period of time. Unfortunately, what might be happening is there may be continued abuse. So that being said, I think we have the luxury of time where we can do our due diligence during that draft process, which could be three months, six months, to a year, depending upon how convoluted the policy may be or the subject matter. So I would argue that if the impression I gave was that we're holding a valuable resource up, it's just the opposite; we're doing our due diligence. And in the meantime, it apparently would be a covered service until such time that the policy, draft policy, is finalized and is an uncovered service based upon literature contribution and the experts. Thank you.

Dr. Patrick Mann

Thank you, Dr. Block. Dr. Regan?

Dr. Terrence Regan

It was brought up by one of the other participants about getting sent from nursing homes and other things like that. I mean, one of the questions here is-- most of these tests, for the present time-- I think everybody is in agreement, and we've talked about it in other questions. These are generally not used for routine testing. So to avoid it being used in routine testing, etc. - and I know that there are some other policies that restrict its use to certain specialties - there could be some consideration of that to have some control over it and then have each of these specialties perhaps come up with different protocols about who are the patient populations that they would deem reasonable for testing. I know we've developed LCDs in that light. As Dr. Block was saying, that's how some of these have been developed in the past. And I would agree with that. But I think that the key here is that we're using these for the complex cases and the complex patients. And they're coming to all of us because it's not routine. The routine testing hasn't found what the problem is. And I think that that's why, at the present time, until there may be changes on how we do these, perhaps it should be restricted to the specialties who use them and deal and treat with these complex patients and beneficiaries. Thanks.

Dr. Patrick Mann

Thank you. So I don't see any other hands up for this last question, and we still have a little bit of time left for this meeting. What I wanted to do now is I wanted to open it up to the panelists as a whole for any other comments or thoughts that you wish to bring up that haven't been addressed by the questions here and/or ask some more questions of your own so that-- and then any of the panelists that we haven't heard from, if they have any comments on any of the questions that have been reviewed over the course of this meeting, we still would love to hear from you. Finally, before I start answering some of the raised hands, we will consider the information and expertise provided today. We would really appreciate it if there are additional thoughts that weren't amenable to discussion verbally but are better written out. Please, send that to us through Heidi DeDay's email. And we will review what we have to determine if LCD development is warranted and post the proposed LCD should we decide development is warranted for public comment and an open meeting. And please, continue to watch our website for additional information. Okay. So for the final sets of comments, we'll start with Dr. Block.

Dr. Mark Block

Yeah, I'd like to make some closing statements here. Number one, I think this is a very interesting alternative or additional tool that we have in our armamentarium. But my concern is that there is abuse and overutilization, and I think that needs to be reined in. We don't want to see the baby thrown out with the bathwater, so to say. So I think if there was a policy that moves forward with this - I'm preaching to the choir - obviously, the abuse has to be addressed. I don't think it's a first line of treatment or analysis, in most cases. I think there are other means that are more appropriate and cost effective. That's number one. And just in closing, in going through these articles, I came across something by a Dr. Bartlett who, quote, said, "Just because you can does not necessarily mean you should. Clinical impact and cost-effectiveness analysis prior to adoption in the clinical setting to avoid the fear of production of a substantial amount of useless information at considerable cost." And I think that's kind of what we're tasked with right here and now. Thanks.

Dr. Patrick Mann

Thank you. Dr. Regan?

Dr. Terrence Regan

Yeah. One of the things here is - and I think everybody's pretty much saying it - we want to have the appropriate use for this. And I think one of the problems is the way some people bill for it, stacking all these codes. And it may be more appropriate to have a appropriately sized or appropriately paid-for panel, a panel that is large enough to cover all of the organisms that may be involved and eliminate the issue with stacking of codes and just have an appropriate-paid panel. I think that would be something that you guys might want to consider.

Dr. Patrick Mann

Thank you, Dr. Regan. I am not currently seeing any other hands raised. I can definitely wait for a minute or two for anybody to want to compose their thoughts and want to say something additional. But again, I would like to thank all of our panelists profusely for their input and their time in making this a very productive and very informative meeting.

[silence]

Okay. With that, I will bring a close to the meeting. Again, we thank the panelists for their time and their input. And any additional thoughts, especially if they come to you overnight in your dreams, please send them our way via Heidi DeDay, and we would love to continue to have this discussion and to further solicit your expert thoughts and opinions. And thank you very much to all.

[silence]