NATIONAL QUALITY FORUM

Moderator: Ashley Morsell
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Ashley Morsell: Good afternoon everyone. We want to thank you for joining us. So good afternoon, good morning – I am sorry. We want to thank you for joining us today. To do the review of this measure, 0255, Measurement of Serum Phosphorus.

You should see on your screen a copy of the agenda that we sent out. Just to go over it, I'm Ashley Morsell. I work here at NQF. I'm a program manager, and specifically I work in measure maintenance. And I'll kind of be facilitating today's call with my colleague, Karen Pace. So that suffices that.

So welcome, we're going to go around to do introductions. I'm going to provide some background information on the Ad-hoc process itself as well as the measure that we'll be evaluating today.

Then Dr. Karen Pace will get into the evidence and sub-criterion as it pertains to this review. We will allow time for our colleagues from the Kidney Care Partners to speak to their stand for requesting this review but we will also allow time for CMS to provide a response.

Thereafter, we'll get into a discussion of the materials that we share with you guys, ask the expert panel and answer the questions that we post. Following that, we allow for any public comment. And then we'll get into you guys making a recommendation on the measure and the next steps.

So like I said, I'm Ashley Morsell. I work here at NQF and I'll have my other two NQF colleagues, Dr. Karen Pace and Elisa Munthali to introduce themselves.

Karen Pace: Hello, this is Karen Pace. And thank you all for joining us and for the panel members for agreeing to help us out with this. And welcome to our KCP and CMS colleagues and Lisa.

Elisa Munthali: Hi, this is Elisa Munthali, managing director with the Performance Measurement Department and I work very closely with Ashley Morsell on measure maintenance. Welcome and thank you for joining us.

Ashley Morsell: So at this time, if we could have the panel members go around and introduce themselves.

Jeffrey Berns: This is Jeff Berns, a nephrologist at the University of Pennsylvania in Philadelphia.

Andrew Narva: This is Andy Narva. I'm a nephrologist at NIH.

Greg Miller: This is Greg Miller, I'm a clinical chemist, direct the clinical chemistry laboratory at Virginia Commonwealth University.

Debra Hain: Hi, this is Debra Hain. I'm a faculty at Florida Atlantic University and nurse practitioner at Cleveland Clinic Florida.

Ashley Morsell: OK. That's it at this time. We'll have our CMS colleagues introduce themselves.

Mary Pratt: Yes. This is Mary Pratt, CMS. I'm the director of the Division of Chronic and Post Acute Care in the quality measures and health assessment group. I work with Joel Andress who is furloughed today.

(Caretta Bird): Hi this is (Caretta Bird), I'm with CMS as well and I work in our quality measures (inaudible) area and I do a lot of support work (inaudible).

Joe Messana: And this is Joe Messana from the University of Michigan. I'm a CMS contractor and I was asked to join the call by Joel Andress.

Ashley Morsell: And anyone else on CMS on the line? No? OK.

At this time we'll have our colleagues from Kidney Care Partners introduce themselves.

Lisa McGonigal: Hi I'm Lisa McGonigal and I'm a health care colleague and I'm with the Kidney Care Partners. We also have on the line some of our colleagues from Fresenius Medical Care.

Eduardo Lacson: Hi I'm Eduardo Lacson Jr., nephrologist, Fresenius Medical Care.

Nicholas Brownlee: Hi. I'm Nick Brownlee. I'm president of Spectra Labs, which is the division of Fresenius Medical Care and I'm a board-certified clinical chemist.

Ashley Morsell: Is that it? OK. OK. Now, we want to keep things moving, what I'm going to bring up now is the, the slides that we had prepared for you guys for today's call.

And let me just adjust the, the view.

So, the objectives for today's call are as follows. We want to first review the request for the Ad-hoc review in the measure developer's response. We also want to evaluate the evidence to support the request for change. And lastly, we want to make a recommendation regarding our request for change and provide a rationale based on the NQF criteria.

So the evidence supporting this measure, these on this slide are the criteria that we had that any request that we get here at NQF has to meet in order for us to be in this Ad-hoc review viable? The first one is that the evidence are put in a measure of practical event has changed and it no longer reflects, updated evidence.

The second one is that there is evidence that implementation of a measure or practice may result in unintended consequences. And what we mean by that is use of the measure or practice may result in inappropriate or harmful care and/or the measured performance scores may yield invalid conclusion about

the quality of care. Examples of such are misclassification or incorrect representation of quality.

In our last criterion is that material changes have been made to a currently endorsed measure. So you see here that the second bullet is bolded. This is the criterion at this particular request is met and with the ground floor as we're moving forward with this Ad-hoc review.

So the process is such that we here at NQF receives a request for an Ad-hoc review and we do an internal review to determine whether or not the actual review meets one of the criteria. At the point that we determine that, the request does meet the criteria and we'll solicit technical experts from previously convened committee and if necessary, we have an additional call for nominations to fill any gaps and maybe identify for no less than 10 business days.

At that point, the selected technical advisors will review the evidence and provide input to CSAC so that suffice – this call today, suffices that the review method selected technical advisors will be going.

After today's call, the information that we aggregate from today will be forwarded to our Consensus Standards Approval Committee or the CSAC, including an assessment of the technical advisors, any public comments that we will receive, an input from the measure steward.

So we just wanted to provide some information regarding this particular measure. So here we have the description of the measure. The numerator statement, the denominator statement and the included exclusion. And you'll see we have noted here that in the numerator statement, it is requested that there'd be a change to include plasma phosphorus.

So Karen, I'll let you take over from here.

Karen Pace: OK. Thank you. So, although the request was submitted under the criterion of that unintended consequences that really depends on evidence that the plasma phosphorus testing would be equivalent to serum phosphorus assessing. And so, that's why we wanted to really focus on the evidence

criterion and this is just a refresher, many of our panel members served on prior NQF committee. So this is probably familiar but wanted to just remind you about our current evidence criterion and basically for a process measure, we want to see a systematic assessment and grading of the quantity, quality and consistency as a body of evidence, that the measure process leads to a desired health outcome.

Next slide.

So, some of the key question – the key questions that we would like the expert panels to think about is, does the evidence for plasma testing of phosphorous meet the NQF guidance related to quantity, quality and consistency of a body of evidence and if not, should not an exception to the evidence be considered, and if so, why? But also thinking about the measure as it's currently constructed.

What is the evidence that supports the current guidelines that specify serum phosphorus testing? Why do those guideline recommendation specify serum testing, both the national and international guidelines? They're very specific and stating that should be serum testing. And does the evidence for the guideline recommendation even address serum versus plasma testing? So we'll get into that when we get into our discussion.

Next slide.

So, we can maybe come back to some of these slides about the details of our guidance on evaluating the quantity, quality and consistency of the evidence, if there is actually that kind of evidence in terms of how it meets our rating scale. But, this is the slide about the quantity which is actually just the total number of studies, not articles or papers. And keep in mind, we're talking about a body of evidence, not the selected studies.

Next slide.

The second area is the quality of the body of evidence which relates to the certainty or confidence in the estimates of benefits and harms to patients

across the studies in the body of evidence. And again, we have a rating scale of high, moderate, low or, insufficient.

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And obviously, most of the quality issues relate to study factors, study design, whether the evidence is direct or indirect to the specific measure focus and the precision or imprecision of the confidence intervals.

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And then the third area is consistency of results for the body of evidence which talks about – is related to the both stability and both the direction and magnitude of the benefits and harms. And again, we have a rating scale. So we can come back to these if we need them. And then we have a decision logic for whether it actually passes our evidence criterion. At any time, there is inconsistent evidence, we would say, "No, it doesn't meet the criterion." But then, there are different combinations of quantity and quality that can still meet our evidence criterion.

Next slide.

And we do have a potential exception to the empirical body of evidence for process measures. So it's actually on the second row there. And again, we'll talk about that as we need to.

Next slide.

And this is some of our updated guidance to really help us work through whether there should be an exception to the evidence or if there is evidence but it hasn't been submitted with the summary of the quantity, quality, and consistency which is our current situation. And again, we'll come back to these to help guide our discussion if we need them. But we'll go on for now.

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And this may be our – the situation that we're dealing with which is empirical evidence submitted without systematic review and grading of the evidence. And again, we'll come back to this if we need to.

Next slide.

And then these are the questions that we will work through if we want to consider an exception to the evidence. And we'll also come back to any of these slides as we work through our discussion.

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Ashley Morsell: That's the end of the slide presentation.

Karen Pace: OK, great. So, what we want to do before we get into our – just to kind of frame how we're going to work through this is that we are going to ask Lisa McGonigal from Kidney Care Partners to give a brief introduction to their request for the Ad-hoc review. And I've asked both Lisa and CMS to try to limit their prepared remarks to five to seven minutes so that we can – if the panel has any questions for them, we can get that in and make sure we're all in the same page. And then after that, after both those presentations and any clarifying questions, we will ask the expert panel to discuss their – the request and specifically to get at the question of the evidence.

So, with that I'm going to stop and certainly when we get to the expert panel discussion, we can clarify any of our criteria about evidence as well. So, Lisa, do you want to give us overview of your request?

Lisa McGonigal: Karen, can you hear me?

Karen Pace: Yes.

Lisa McGonigal: OK, sorry, hold on one second. I'm getting an echo down here. OK, my name is Lisa McGonigal. Again, I'm a healthcare quality consultant to Kidney Care Partners. This is a background. KCP is an alliance of members of the kidney care community that serves with the forum for patient advocates, dialysis care professionals, providers and manufacturers wherein everyone come together,

all of these stakeholders and work together to advance policies that support and allow for the creation of high quality care for individuals with both CKD and ESRD. We've been long-term members at NQF and we've been pretty active in all of NQF projects related to renal disease.

So first, I'd like to thank both NQF and the Ad-hoc channels for convening to consider this request on the review of our measure 0255 measurement of serum phosphorus concentration. So again, as actually and Karen have mentioned we requested this review on the basis of NQF Ad-hoc review criterion number two, implementation of the measure results in unintended consequences and in this particular page, we're concerned it is drawing invalid conclusions about the quality of care.

So it's currently specified on measure – 0255 requires at dialysis facilities a test that they've monitored, each of their Medicare patients' serum phosphorus levels monthly throughout this performance period, and the issue at hand here, is that the measure requires testing be done on serum and failed to recognize plasma as an alternative testing substrate. So this is problematic because as you all well know, dialysis facilities are subject to the nation's first (inaudible) only penalty based quality performance program. KCP has very real concerns that implementation of this measure as is currently specified are one of only five measures on which dialysis facilities' performance is being judged for payment year 2014.

We have significant and negative financial consequences for each facilities that use plasma as its substrate. These facilities would be unable to attest them to the measure as specified that they measured monthly serum phosphorus and consequently they did not conform well on the measure. We also note that adoption of a measure that recognizes only serum phosphorus measurement within the ESRD QIP would indicate a preference in the regulations for a particular testing method. And to solve this issue, KCP believes that the specifications need to accommodate the industry expected standard measurement of the both serum and plasma phosphorus. And we're requesting that NQF seek to change to the measure specification side of the developer to reflect this.

So at present we're aware that (inaudible) renal laboratory and Ascend Clinical that's using plasma testings since 2006 and others, for example Spectra Laboratory are also considering the change. In regards to equivalency, we noticed that serum and plasma testing have been validated from most clinical chemistry analyzers and both have been deemed acceptable by the analyzing manufacturer.

So our colleagues at Fresenius Medical Care who are also on the call today, and they are able to answer some of the questions on the testing as well as a lot of experts who performed some of the test that's were submitted to NQF and the channel.

They studied the differences between serum and plasma samples from phosphorus on a group of ESRD patients. And they demonstrate that there is virtually no difference in the result. The average of difference is less than 0.01 mg/dL which is essentially negligible considering the phosphorus that's customarily recorded to the nearest 0.1 mg/dL.

As Karen brought up recently, I do note that Fresenius makes that some complications are found in serum values that can be higher than plasma at actually 0.2 to 0.3 mg/dL. This occurs if phosphorus is released on serum while clotting.

However, such differences that were seen on the college, are the American pathologists' total allowable error and the differences could not be replicated by (inaudible) experiment conducted by Spectra Laboratory.

In addition to yielding equivalently the results to serum plasma also required loss of blood, is the most stable and required serum manipulation (pieces) and needs your recorder software to perform additional testing for – it is definitely more patient friendly, (inaudible).

So this for example, serum samples require that blood be allowed to clot prior to centrifugation over – as you all know in busy dialysis facilities where direct patient care has to take precedence, sometimes there are lapses in sample handling protocols and results at – a lot of samples are unusable because of varying levels of hemolysis. Consequently, many (times) have canceled,

including clinical information is delayed in many cases, this project to repeat blood draw. And all of these issues are essentially eliminated with the use of plasma.

So in conclusion, on the surface, it may appear to be a minor issue. It presents very significant repercussions for dialysis facilities that utilize plasma rather than serum for their testing. And as equivalency has been demonstrated, the serum and plasma phosphorus with (inaudible) is industry-accepted standard. KCP believes that performance measure relating to the measurement of phosphorous should therefore be (analyte) and neutral.

And I just wanted to stop to see if any of my colleagues in (FMC) had anything he wanted to add or clarify before we move on.

Nicholas Brownlee: Nothing to add from me.

Eduardo Lacson: Hi. This is JR and from my perspective, from a quality improvement and process improvement perspective, I'd like to stress the last point made by Lisa whereby in a very busy dialysis unit, despite a lot of education and training, there is always transition of staff as well and turnover. And so, it's hard to keep up and it is inevitable over the last decade despite all efforts that we have thousands of canceled death every month which need – requires a re-draw and requires other things and, you know, doing the same thing over and over again for us and expecting a different result doesn't seem to work.

We needed a process changer and that's what attracted us to plasma because if we don't need to wait for blood to come, then the samples could be centrifuged and sent immediately and it would eliminate a source of error and process variations, and decrease complexity of all the tests that need to be done in the clinic. So, I'd like to stop there and thank you.

Karen Pace: OK. This is Karen Pace. So, before we go on to Dr. Joe Messana for CMS, I'll just ask if the panel has any clarifying questions regarding the comments or the materials that were submitted and then we'll get into discussion after CMS has presented, but just if there are anything that you need some clarifying. Panel members?

Greg Miller: Yes, this is Greg Miller. I would like some additional information about the hemolysis influence. I'm not (inaudible) that – serum versus plasma.

Lisa McGonigal: JR and Nick, we leave that since you guys are the experts on this. Please go ahead.

Eduardo Lacson: So, Nick, would you like to …

Nicholas Brownlee: Yes, no, I will. Yes, hemolysis generally does not affect phosphorous significantly as long as it's slight. Unfortunately, many of the samples that we get that are not handled appropriately in the clinics when they are drawn and process, we have multiple issues with clots in the serum and other issues that's with getting enough sample in order to get a test. Plasma, gets us around.

Greg Miller: I guess I'm failing to understand how plasma solves the problem of either inadequate volume of sample or hemolysis.

Nicholas Brownlee: Plasma, I think plasma does not – well, plasma does get around the issue of hemolysis if the sample is mishandled at the clinic where the samples are drawn and they're – they basically fit in either unspun or in the clot for very extended periods of time usually unspun.

With plasma, there's less of an issue with that one. As far as quantity of sample has to do with, if samples are spun too soon in the clinics, we end up with vibrant clot above the barrier in the SST tubes. And we end up many times with (QNS), not only for plasma but for many other sets of serum test.

Greg Miller: OK. And thank you. One other question, the data that was provided in the – whatever the document name that was handed out. There's a bunch of EP evaluator, graph some changes. Is that – Is that data published anywhere? Is it only provided as part of this submission?

Nicholas Brownlee: Is that – did that data came from Ascend, is that correct?

Karen Pace: Yes. It's the data that KCP is submitted to us.

Nicholas Brownlee: Yes. It came from the sent labs which is not from Spectra which where – I'm from. I don't know that that data is published anywhere and we could certainly – that's something we can find out that I don't know that.

Eduardo Lacson: But to my knowledge, those have not been published.

Greg Miller: OK. Thank you.

Karen Pace: Any other questions from the panel members for clarification right now?

Jeffrey Berns: This is Jeff Berns. I suspect the answer is going to be clear to this. But, have you looked at how often, if you would just switch from the serum to plasma or for dialysis facility, we'll just switch from serum to plasma, that patients would fall above or below, any quality metric or therapeutic professionals?

Eduardo Lacson: Hi, this JR Lacson. From, from our perspective, Spectra had conducted two separate studies internally. One with about 101 patients, the second one is about six months later with about 129 samples are tested both like serum and plasma.

And we were within 0.01 on average. And so, it would not have impacted the results at least within the hands of our laboratory. In the larger contacts with the Ascend results, if you look at their, you know, with over 5,000 samples and they did a comparison, I believe it's in 2008 or something. And if in those 5,000 samples, they found a bias of about 0.1 lower results in their plasma results relative to the rest of the country in the USRDS.

Greg Miller: This is Greg. Is that data available to us, has it been published?

Eduardo Lacson: No, it was data provided by Ascend and for their internal review. And I believe that's been submitted to NQF in terms of what they've looked at internally, but I don't believe it's been told.

Lisa McGonigal: And why is it in the NQF documentation though?

Karen Pace: OK. All right. So, let's move on to CMS. Dr. Messana, do you want to brief us on the CMS discussions? I know there was a tip in those materials were also included in the documentation?

Lisa you received a copy of everything we sent to steering committee, did you not?

Lisa McGonigal: No, actually I did not. I just received slides in the agenda.

Karen Pace: OK. I sent it this morning in my question to you …

Lisa McGonigal: OK.

Karen Pace: It's also, I mean, it's also posted on the website. So …

Lisa McGonigal: Wait.

Karen Pace: And let's go to Dr. Messana.

Joe Messana: So, my comments will be brief and I want to point out that although I was physically present and attended as an observer of the Bone and Mineral TEP that was held last April. Dr. Francesca Tentori from Harvard research was a facilitator.

And so, my perspective on what I heard that that TEP and what I read in the final report afterwards was that the test was basing their opinions on plasma versus serum, largely based on the national-international guideline and the absence of published literature supporting the specific use of plasma in ESRD patients, right.

It's not clear to me how much of the industry quality data that they were able to review before the meeting or how much that sways them or where do they focus more on the literature. And I know there was a bit of discussion about the similarities between serum and plasma literature values for phosphorus and the general population, but there was quite a bit of concern expressed by TEP members about the lack of a specific published literature relating to whether being general population result could be extrapolated to ESRD patients. And I guess that's probably one of the central issues for the discussion here today.

Their recommendation was clear and that they did not feel as a group that plasma should be substituted for serum at this point based on the reasons that I have discussed. And I think I'll leave it at that. As an individual practitioner, I'd certainly recognize the operational efficiencies and potential improvements that might be associated with using plasma rather than serum in a dialysis facility. Dialysis units are hectic places and handling of specimen and preparation for shifting with centralized laboratories is not a perfect operation despite efforts from the national providers to try to improve that situation.

That concern or concerns about that process in data handling and delays and what not, were discussed and were part of the deliberations of the path at that time and they were interested in seeing more information, to review the information particularly but more information relating practices in dialysis facilities to the general literature looking at serum and plasma. Thank you.

Karen Pace: OK, and does the panel have any questions for Dr. Messana or CMS colleagues? And we did include their test report in the materials we sent to you and in the large PDF documents that is one of the tabs. So, any questions for Dr. Messana or CMS from the panel?

Greg Miller: This is Greg Miller. I have a general question about dialysis. I don't know if it's necessarily directed …

Karen Pace: OK.

Greg Miller: … to individual.

Karen Pace: OK.

Greg Miller: My question is when patients are undergoing a dialysis procedure, do they – did they have a heparin to assist in blood flow and prevent clotting during the procedure? Is that part of the process?

Joe Messana: Most do, there are alternative anticoagulants and dialysis can be achieved without additional heparin but I would say that the standard is anticoagulation after initiation of dialysis. I don't know if JR wants to weigh in on that as well.

Karen Pace: And who is that – that just answered that question?

Joe Messana: I'm sorry, Joe Messana.

Karen Pace: OK, thanks.

Eduardo Lacson: Hi. It's JR Lacson, I agree with Joe most patients do get heparin for their treatments. Most of the time, the phosphorus and other analytes are drawn prior to receiving that. This is done predialysis.

Joe Messana: This is Joe Messana. I concur with the JR's division as well.

Karen Pace: OK. So that's the situation that we're dealing with. So, I think it does come down to, you know, some discussion about the evidence and just one question I think this has already been asked but to KCP, you submitted the unpublished data from one laboratory I believe.

And so, just to clarify and confirm, you did not find any published evidence or systematic reviews of evidence that addresses this particular topic, is that correct?

Lisa McGonigal: Hi. Yes. That is correct, this very new and therefore I'll be letting Debra (inaudible).

Karen Pace: OK.

Lisa McGonigal: And, yes, JR, correct me if I'm wrong, but I believe that's the case.

Eduardo Lacson: Hi this is JR, just one additional point. I believe that what the key point is that there is no published evidence at least in the endstage renal disease population, but in the general population and I believe our expert chemist will know more about this, but in hospital labs and in other settings, this has been sound to be (equipping).

Joe Messana: Well, Karen, this is Joe Messana from University of Michigan. I would like to respond if I can.

Karen Pace: Yes.

Joe Messana: So part of the preparation from the top as many people know who's been through them is an exhaustive literature review looking for any peer-reviewed study as well as guidelines in preparation both for the testament for subsequent measure specification.

We did not find any literature pertaining to this topic directly in ESRD patients. I agree with Dr. Lacson that there are several older being, 1970s, 1980s studies looking at plasma versus serum, small studies that suggest small systematic biases with serum being slightly higher than plasma.

But our test, and I think there is even some discussion of one or two of those articles when top discuss this and they were concerned that – they were concerned about extrapolation from what's available in the literature which is general population to ESRD-specific settings.

Karen Pace: OK. So I'm going to stop there and would like to have discussion among our panel members now, and to get your thoughts about, you know, the evidence that does or does not exist, especially in light of the fact that the published guidelines both national and international specify serum, whether your knowledge about this that that was intentional and if you have any knowledge about that.

And also, I have, you know, suggestions for how the panel may want to work through this and also if you have any questions for me about NQF evidence criterions.

So, I know this is a little more difficult on the phone but maybe I'll just ask if starting with Jeff Berns if you want to make any comments to your colleagues on the panel.

Jeffrey Berns: Sure. My initial response I think was to figure that this is a miniscule difference and probably not a consequence. But as I'm now looking and this is on page 34 of – out of 103 pages (inaudible) …

Karen Pace: OK, let me ask Ashley to go ahead and bring up that document and we can, you know, show that so that – you can go ahead and keep tracking but I'll – what page do you want her to go to?

Jeffrey Berns: Ten – which is pages 34 – page 34 – 33 and 34 out of a 103.

Karen Pace: OK.

Jeffrey Berns: And then – and there's a conclusion. This is in the text I guess on page 33 that – and so if you cancel to reflect 9 percent of the population, which should be shifted from the 5.1 milligram or less in laboratory admirals to 5.5 milligram are great in the laboratory (inaudible) and I'm not (inaudible) if laboratories were measuring one-on-one measuring the data. And then in figure 10 over on the right-hand slide of that curve or that figure 5 we're reading it correctly. Let's turn them around maybe just under 5 percent to approaching 10 percent depending on which bias one is looking at would be potentially affected at target concentration.

So, although the error, the difference between the assays is small, it does seem as if there's a significant percentage of the population that have potentially – would be potential impact, like a serum in the ESRD population. I'm not sure this does any harm in a result from that, but I don't know that it wont either.

Karen Pace: OK. And I'll move on to Andy Narva. Do you have any comments or (inaudible) …

Andrew Narva: Yes – no. I think I'm understanding it's similar to how Jeff did, my initial understanding was that this was a trivial difference and the fact that there is data available in ESRD patients and there's a possibility that it could make a difference in this concern.

Karen Pace: OK. And Debra Hain?

Debra Hain: Hi. I can quote the previous two members of the panel that is – either it's just a lack of evidence with the ESRD population. But yet, there is not really substantial that evidence to support that it will harm them and I mean even that small amount, but then, here are those concerns as mentioned previously.

And then the – as a clinician, I do understand the operational issues and the inaccurate specimen handling and preparation, and so, how that can lead to inaccurate results with the phosphorus and I see it in my own practice as I round in dialysis centers.

Karen Pace: And Debra that the point of that is that with plasma, you think there's lots of mistakes with the handling? Is that …

Debra Hain: The way – from what they're telling me, I don't see that as there's no evidence to support that, just based on what I heard from previous, from people …

Karen Pace: OK.

Debra Hain: … presenting and the documents that were sent to us. But I don't really see, you know, there's a lack of evidence to support that because as you all know, the studies are showing just a serum. So – but – so I'm not – I can't – I only know there are errors made and based on the people who said – have said that that may make the difference. But I don't know for sure.

Karen Pace: OK. And Dr. Miller? Greg Miller.

Greg Miller: Yes, I have a few comments I'd like to offer.

I think the difference between serum and plasma phosphorus in non-end stage renal disease patients, which is the only available evidence is moderate, usually in the literature, it comes out at 0.1 or 0.2 mg/dL found in various studies that have been reported.

What I'd like to answer or offer is that those are trivial differences in the light of the biological variability of phosphorus in blood in reasonably normal people, there's a parameter in lab medicine called the relative change value, which is a statistic that's computed based on the analytical coefficient and variation for making the measurements and the – within individual coefficient and variation for, you know, biological variability.

So, the data, if we just accept that the labs can measure phosphate with about a 2 percent coefficient and variation, which is actually a very good

performance, the reported biological variability is about 8.5 percent, which dominates the calculation.

So, if you do the calculation on the phosphorus value of 4.5 mg/dL, it is about the amount of difference in phosphate that is clinically meaningful as close to 1 mg/dL, which indicates that the small difference between serum and plasma is relatively unimportant in reaching a conclusion regarding the patient's condition. And that's in, you know, people who have reasonably normal phosphate physiologic conditions and so that's, you know, one observation.

I think if you extrapolate to the population that are undergoing dialysis, their biological variability is going to be much poorer. And so, the difference that will be clinically meaningful becomes even larger relative to the minor difference between serum and plasma.

The other thing I'd like to point out is that I just happen to stumble across the Australian recommendations for collecting specimens and they'd recommended heparin plasma to measure phosphate in their online manual of general laboratory procedures. Those procedures are not aimed at dialysis or end stage renal patients, they're just general recommendations for measuring phosphate. So there's some evidence internationally that heparin is an approved subtype.

So, the other comment I'd like to offer is that the fact that a manufacturer of a phosphorus measuring procedure tells you that it's OK to measure either serum or plasma should be interpreted that the measuring procedure itself will give a correct value with either sample type. It does not really address a recommendation for which sample type to use and the important thing is are there significant differences in the results when the different sample types that would affect clinical judgments.

So, you know, given what we've seen so far, I think it's a fair statement to say that in an end stage renal disease population undergoing dialysis, there is no evidence that plasma wouldn't be an acceptable sample.

So, that's the end of my comments.

Karen Pace: OK. And so, Jeff and Andy, in light of what Greg just stated, how does that impact what you were thinking in terms of the table that you referred, the figure that you were referring to? And do you have any follow up questions or anything to clarify or discuss?

Jeffrey Berns: I don't have anything for that. I think it's, you know, there's sort of a conundrum here. You know, the tests are very accurate. The tests are very, very similar. But based upon non – you know, there's not robust testing in the ESRD patient population.

So, we're left with the data that's somewhere between 5 percent and 10 percent of patients will have measured serum phosphorus on a different side of the cutoff now, again, whether that is clinically relevant or not one could argue, but recognizing the treatment decisions about phosphorus binders, calcium and so forth, are made rightly or wrongly based upon these minor trends. You know, it has a chance to change how patients are managed.

My recollection, if I can just ask a question to clarify is that the phosphorus measure looks at three months rolling average for single month. I just don't recall ahead.

Karen Pace: Joe, can you answer that and we can pull up – and, Ashley, if you would pull up the specifications but Joe Messana, can you – well, let me just say. This measure is just about the getting the monthly sample, just so …

Jeffrey Berns: I understand but the impact, you know, so it's a little bit above or below in one month from an average over a course of three, it's not, and it becomes less important.

Karen Pace: Right. So, I understand what you're saying but I'm just mentioning that we ended up not endorsing that performance measure about the actual phosphorus level.

Jeffrey Berns: I was just – that's fine then.

Karen Pace: Yes. Joe, do you want to add anything?

Joe Messana?

Joe Messana: That's right. I'd be wasting time. That's correct. This is a measure that was a process measure. Are you measuring phosphate – serum phosphorous, excuse me, on a monthly level – on a monthly basis? It did not specify a target range.

Jeffrey Berns: OK. I got it.

Joe Messana: Whether you are measuring.

Jeffrey Berns: Right.

Karen Pace: Right. But, Jeff, you're right. That's one that we did that in the last project, did take a look at a measure that way. But, ultimately, it wasn't recommended. Obviously, the goal would be, you know, exactly what you're talking about, to look at the actual values and hopefully in the future be able to have a more specific performance measure based on the management.

But at least, a couple of years ago, when the committee reviewed that, they didn't think the evidence supported the particular cutoff.

Andrew Narva: Karen, we're not allowed to request additional data or suggest that additional data be collected or can we make that recommendation?

Karen Pace: We can talk about it. We have that, you know, certainly, you know, if you think there's something that would help us, you know, move in the right direction, we can certainly entertain that.

So, what is your thought?

Andrew Narva: I, you know, I – is it possible to get or to collect more data to show where you would get both plasma and serum data on a large number of people actually on dialysis.

Karen Pace: OK. And let me just double check also with Lisa on the information that you submitted to us from – I believe it was just Ascend with that, specifically, ESRD patient data?

Lisa McGonigal: I'm sorry I was on mute. I believe that was …

Andrew Narva: OK.

Lisa McGonigal: … ESRD specific lab, is that correct JR and Nick?

Eduardo Lacson: Hi. This is JR again. Yes, I'd like to clarify two things. One, the variability of ESRD lab study which I heard was referred to earlier in page 33. That was eight end-stage renal disease laboratories that correspond to probably 80 percent of all patients and they compared their laboratory testing.

Most of those are doing serum. So, the (inaudible) and the variances that they're observed are whole between laboratory using serum and the variance there dwarfs any differences in plasma and serum measurement (inaudible) so I just want to make that point.

The second is in the literature on in general lab, most of the study samples are between 20 and above 60 patients. So, when the request was made for more data in ESRD for a large number of samples, how do you define large?

Mary Pratt: And yes, I see what this is, so that this was the – they used a specialized group of ESRD testing lab with the information that we submitted to you.

Karen Pace: Right. But so the clarification was on those tables about the variability that we followed that serum testing and variability between labs, is that what you're saying, JR?

Eduardo Lacson: Yes. Yes, ma'am. That's what's in that big study of ESRD, eight ESRD laboratories.

Karen Pace: OK.

Eduardo Lacson: And the reason why I asked how you define large is because large is a relative term. The data that we have right now in ESRD from a sense, they – I think only tested, I don't know, 50 samples paired and then they also looked at their total, I think that Ascend, their clients comprise mostly of (inaudible) dialysis chain. They looked at about 5,000 samples and compared their plasma test to the overall distribution in USRDS.

So, that's one lab. Within the Spectra testing, we have conducted two internal studies and to me which I consider large, which is the first one, is about 101 patients. And the second is 129. These are all paired ESRD samples. Now, the problem is they're not published and I send – and I take an action feedback but I just wanted to let this be classified as yes, to me those are two large separate studies in addition to the ongoing clinical experience over eight years now of Ascend Clinical Laboratory with thousands and thousands of ESRD patients.

Joe Messana: Karen, if I may, this is Joe Messana.

Karen Pace: Yes.

(Joe Massa): The only point related to JR's comment that I would make is that the initial experience, the paired comparison for Ascend were I believe 54 samples if I read the information correctly. The subsequent comparison was the distribution of plasma phosphorous compared to historical controls within that organization and the utility of that is somewhat limited by potential changes and practice patterns and underlying shifts related to longitudinal changes in those practice patterns, but I agree with the numbers that JR stated them otherwise.

Karen Pace: OK. So, Andy, in terms of the more data, so Joe, you're pointing out that the actual paired samples with only 54 and, Andy, is that what you're referring to having more data in terms of actual serum and plasma from the same individual so that you can do that.

Andrew Narva: Actually, I found it a little confusing about whether – which parts of the data we're comparing apples to apples and which we're comparing apples to oranges, but – I don't know, I – the sample you said should be big enough to determine whether or not there is a significant – it doesn't seem like there is.

Karen Pace: Right.

Eduardo Lacson: I'm sorry, if I may speak.

Karen Pace: And who is this again?

Eduardo Lacson: This is JR Lacson for further …

Karen Pace: OK.

Eduardo Lacson: And that's the reason why I asked how large was going to be defined because the Fresenius sample of patients there was 101 in one study and six months later 129 patients with paired testing of serum samples in the ESRD.

And that's where we got that value. In one test the sample bias was minus 0.01 and in the other was plus 0.01 and so they cancel each other out. This is spot on at least in that kind of Spectra laboratory.

Karen Pace: And can you – I'm sorry, I don't know. Lisa, can you direct us to where in the materials event that JR is referring to?

Greg Miller: There is a table on page 25 of the 103 in the Power – in the …

Karen Pace: In the PDF.

Greg Miller: Yes. Is that the table that you're referring here? It's comparing Neptune, Commodore, Admiral, (Castrol), Eagle, Mariner, Tern and Gull. I don't know if (inaudible) the different laboratory (inaudible).

Eduardo Lacson: That's right.

Karen Pace: So yes, I believe that's it on page 25, JR?

Eduardo Lacson: No, no. That's – all that data that they're referring to with those code names Commodore, Admiral, those are all the tests of eight renal laboratories (inaudible) samples for whatever assay they're all using. And seven out of the eight labs are using serum testing, only Ascend small number relative to the whole is using plasma test.

So the overall variance (inaudible) variation that you see reported between laboratories reflects variability implementation of the assay for serum for the most part. So what I'm referring to and I'm not sure if you receive this but we

had sent this out to at least to CMS and to, I thought the NQF (inaudible) conducted a study in two time periods, six months part, one with the sample of 101 patients and the next is a sample of 129 patients. Jeff would inspect the laboratory and tested the paired samples.

What I was referring, I'm not sure, I don't have a copy of what packet you received so I can't tell you what page or if it's in the packet or document but there is data in those combined trials of 230 ESRD patients, in two studies that we did internally.

Greg Miller: Is it – this is Greg. Can someone determine if that data is in fact available to us while we're on the call?

Karen Pace: So, JR you are online?

Eduardo Lacson: I could send out an e-mail, Nick, if you don't mind.

Karen Pace: No, no, no, no. Before you do that, I want to see it if it's in the materials that Lisa sent us. So …

Lisa McGonigal: Yes, give me one minute, OK?

Karen Pace: OK.

Lisa McGonigal: Karen, if you want to continue we can come back to this.

Karen Pace: OK. All right. So, and maybe Greg, you can talk more to this. I think this is somewhat of what you were getting at to. I think their point is that there's more variation between labs using serum testing than the variability that results when you're comparing serum to plasma. But I think the question from the group whether we have much data to look at the difference between plasma and serum specifically in ERSD patients.

Am I understanding that correctly?

Greg Miller: Yes. This is Greg. Yes. I think that's correct. I'm just looking at another paper that was published in 2008 which haven't been shared with a group but the study was – in the cause of American pathologist, they included a serum

sample and compared results among and I forget the exact number but I'd says it's about 20 different measure procedures in use throughout the United States and the difference in mean value among the different measuring procedures themselves is about between three-tenths and fourth-tenths of a milligram per deciliter for the average value of the labs that submitted results.

So I think the variability between methods and between laboratories is greater and the variability between serum and plasma, and I think the data that was just described as two studies of 100 and something samples each where plasma and serum were paired would be extremely important to help us understand the magnitude of that actual difference in this particular patient population.

Karen Pace: OK. Right. So, Lisa, what I have was that you sent me the study that we were talking about the variability between labs and then the supplemental things that you sent me on my second request was about I think the – actually, if you go to the pages, a couple of pages right before the second sector.

Lisa McGonigal: Yes, I was looking at page – title page seven at the end of the – that is some (inaudible) so the text is an appendix. The specific information based on laboratory validation studies comparing (inaudible) plasma sample testing and serum sample testing performed by Spectra.

Greg Miller: Can you – excuse me.

Karen Pace: What page of the PDF are you on?

Lisa McGonigal: It's on page seven of the PDF. Seven of 45 (inaudible).

Greg Miller: You have to look at the PDF page …

Karen Pace: Yes, look at the PDF page number please.

Greg Miller: Up in this big.

Lisa McGonigal: OK.

Greg Miller: In the upper, at least on my computer, there is a PDF page number scroll thing on the top of the ribbon.

Lisa McGonigal: OK. Wait, one second. OK. So here it would be on page – my goodness. Yes, I don't have the number though.

Karen Pace: You have the PDF open, Lisa?

Lisa McGonigal: Yes. I do.

Karen Pace: Well, there's a PDF page number by your up and down arrow, page arrows.

Greg Miller: (Inaudible) top of page 11, PDF.

Lisa McGonigal: Yes, that's right. Yes, page 13, one, three.

Karen Pace: OK.

Lisa McGonigal: Does that help?

Karen Pace: Yes, actually. I got it.

Lisa McGonigal: OK. And JR, you need some – this is what you're referring to here.

Eduardo Lacson: I'm sorry, I don't have the document that you have.

Karen Pace: Are you online, JR? I mean are you on the webinar?

Eduardo Lacson: No, I am not.

Lisa McGonigal: You're not. OK. So the (inaudible) is – all right, in appendix, additional specific information based on laboratory outpatient study comparing last plasma sample testing and serum sample testing performed by (Inspectorate) laboratory. Then it has phosphorus and calcium. CLIA allowable total error that has allowable error is 0.3, (inaudible) 0.2 percent. Is this what you're referring to? I sent you this. Is that it?

Eduardo Lacson: That is the overall result that we have and in fact we submitted that as an appendix to CMS for both phosphorus and calcium testing. And I have the

actual spreadsheet result that delineate, you know, the mean, the standard deviation, and the (special variance) and all of that if you want it.

Karen Pace: OK.

Greg Miller: This is Greg. I think that's the information that we're actually trying to get which apparently we don't have in our documents.

Eduardo Lacson: And I thought it was. I apologize for that.

Karen Pace: Yes.

Eduardo Lacson: But the number of samples in those two studies, the first one is 101 patients for our samples and the second one is 129. And the first one – they're six months apart.

Karen Pace: Are you talking about the two studies, phosphorus versus calcium as two studies or because we only have …

Eduardo Lacson: Because if you look at the last bullet point under phosphorus it says (bias).

Karen Pace: OK.

Eduardo Lacson: ST which is plasma minus SST which is the serum test and two experiments, the first sub-bullet is in 101 samples, the second is in 129 samples.

Karen Pace: OK. All right. So, Greg, you would like to see the whole data is what you're saying. We can certainly get that and …

Lisa McGonigal: JR, just send this to me and I can forward it on to chat.

Eduardo Lacson: I will send it right now.

Lisa McGonigal: OK, great.

Karen Pace: OK. And let me just ask the panel because I know many of you follow the guidelines and as I mentioned, and also in your briefing memo had checked to see what the current guidelines are, and I think Dr. Messana also mentioned this that both the national – the KDOQI and the KDIGO guidelines to specify

serum levels. So, does anyone have any insights into the decisions that were made in producing the guidelines in that manner or is there anyone we should be checking with on that?

Jeffrey Berns: Yes, this is Jeff Berns. I can't imagine to even consider plasma, just assume that where everybody was measuring was serum and that was what's considered and that's what's reported in the literature in terms of relationship and outcomes.

Greg Miller: This is Greg. I think it's – I mean, the other lab people on the phone can correct me if they disagree with me. Almost jargon to say you're going to measure a serum something or other and, you know, you may or may not actually mean serum. You may mean plasma or you may recognize a plasma and serum gives essentially the same values.

Historically, people made all measurements on serum and it's only been perhaps in the last decade, maybe 15 years of plasma has emerged as a sample that adds value because it can be processed quickly than serum. For example, many hospitals there in acute care settings will refer plasma samples for staph test in chemistry simply because you don't have to wait for them to clot and it shortens the turnaround time.

So I think some of the differences between serum and plasma have grown out of colloquialism in terminology which isn't to say we don't need to be careful that there are differences, there can be real differences, but in many cases, there really isn't any real (inaudible).

So the statement that the guideline writers perhaps didn't even consider serum versus plasma is probably appropriate.

Debra Hain: Hi, this is Debbie. When I'm looking at the studies that were used in the guidelines, they all said serum. So, you're saying that maybe they didn't realize that they had plasma on those? I'm not quite sure. Are you saying that the guidelines may not have realized because I didn't – when looking at the studies, I didn't see anywhere that they said that they used plasma.

Greg Miller: I think the guidelines, it's – were based on serum measurements because that's pretty much the data (inaudible). I doubt they considered whether or not a plasma sample wasn't appropriate substitute for a serum sample.

Debra Hain: OK, thank you.

Greg Miller: I don't know that, I'm just (making) …

Lisa McGonigal: Karen, I forwarded (inaudible).

Karen Pace: Yes, I just forwarded it to the panel members.

Lisa McGonigal: Great, OK.

Karen Pace: But it's – when I open it, there's only one page. Is that correct?

Lisa McGonigal: Right, that's correct. That's the one.

Karen Pace: OK.

Lisa McGonigal: (Inaudible).

Karen Pace: OK. And, Ashley, can you – I sent it to you as well …

Ashley Morsell: I can project it.

Karen Pace: OK.

Ashley Morsell: I just have to stop and bring it up.

Karen Pace: So, I'm sorry. Debbie, you're saying that the studies that are cited in the guidelines, the studies themselves also specifically refer to serum?

Debra Hain: Hi, I didn't look at every single study but the ones I did look at, we're referring to serum because I was specifically looking for did they mention serum or plasma. And from what I saw in the studies that I looked at were – in the systematic reviews were serum.

Karen Pace: OK.

All right.

Andy, while we're on this waiting for Ashley to bring that up, you had shared with me some information about current coding of laboratory test. Do you remember what I'm referring to?

Andrew Narva: No, not really.

Karen Pace: OK. Let's see if I can find it. You had forwarded something to me about them. Let me see if I can find it.

Ashley Morsell: So, I just brought up the document that was shared with this. Do you guys see it?

Andrew Narva: Is it possible that somebody could walk us through that so we're sure that we – those of us who aren't clinical chemists – clinical chemist that much would know what we're looking at?

Karen Pace: OK, are you going to walk people through?

Eduardo Lacson: OK. Again, I'm not a clinical chemist but I'll do my best.

The first problem is the analyte that's being measured. So, you can disregard this option for this particular distraction so that they describe two phosphorus post and the first test – and you will see the third column, the date when the testing was done.

The middle column just provides sort of a standard based on (CAC) 0.3 for phosphorus milligrams per deciliter or about 10.7 percent. So, (CAC) actually has an even wider acceptability range than what we think is feasible for ESRD. So most ESRD labs privately (inaudible) knowing that phosphorous is measured and acted upon in the ESRD.

In the fourth column is the number of patients or in this case, number of samples, paired samples that were tested. And the slope and the intercept in the fifth and sixth column indicate the integration line when you compare one

plasma to serum testing and the R is a correlation. That's column number 1, 2, 3, 4, 5, 6, the seventh column.

The bias column that (inaudible) the direction. So, in one test, in the second row is minus 0.01 milligram per deciliter and in the other is plus 0.01 milligram per deciliter.

So, (inaudible) you have one test swings compared to the other and (inaudible).

Greg Miller: This is Greg. May I ask a question at this point? Do you have – do you know how the bias was calculated.

Eduardo Lacson: I would have (inaudible) …

Greg Miller: It's not consistent with the intercept values and they should be relatively close to each other.

Eduardo Lacson: I'd have to defer to Spectra on that.

Greg Miller: Is there any …

Nicholas Brownlee: We had a consultant. I call the chemist consultant do that so I'm not exactly certain how that was done. That was done through KCP.

Greg Miller: I'm guessing that's 0.1. I think the bias reflects the difference between the mean value of SST and the mean value of PST.

Eduardo Lacson: You may be right here.

Greg Miller: OK.

Eduardo Lacson: And then you've already saw that. That means between the two S for serum and P for plasma, the range of values that were tested based on serum and plasma and then the results. And the others I would (inaudible) for the comments. I mean this document just expands on the summary.

Karen Pace: Right.

Eduardo Lacson: That was on page, I think, 13 that he talks about in the letter we sent to the CMS to provide context.

Karen Pace: Right.

Joe Messana: Karen, this is Joe Messana. May I ask a question related to these data?

Karen Pace: Yes.

Joe Messana: JR, can you estimate how many serum sample measurements per year Spectra labs have for Fresenius dialysis patients? It's to get a sense for how small a sample this was relative to, you know, the ongoing business related to measurement of serum phosphorus.

Eduardo Lacson: I would defer to Nick on numbers.

Nicholas Brownlee: It's basically 200,000 times – well, actually more than – probably 400,000 analyses per month times 12. So, about half a million.

Joe Messana: Thank you.

Eduardo Lacson: But I'd love to put that in context if I may, with all due respect to the panel.

In terms of plasma and serum tests that are coming to us every year in the millions every month and most of the lab studies that have shown equivalents are also small numbers, 50, 60 individuals (inaudible).

Karen Pace: OK. So let me ask the panel what your thoughts are whether you need more information to make a recommendation, whether this is – we need to figure out where to go from here, if you can make a recommendation at the end of this call. We'll have it open for public comment before we get to that point, but I wanted to just do status check and see what your thoughts are in terms of you thinking about this, whether you think you can make a recommendation, whether we need more information and to where you're at with it.

So, I'll stop there and just ask the panel to weigh in and give me some of their thinking.

Jeffrey Berns: This is Jeff Berns. I guess I'm a little bit undecided. I'm not sure if there's any more information. My gut feeling tells me that this is probably not a clinically important difference.

Karen Pace: Anyone else want to weigh in? It sounds like – let me just check my understanding that we've heard from Greg that there may be a lot of interchangeability of whether it's serum or plasma testing that's done. But the only study that we have is this one small study, unpublished study that is specifically looking at serum versus plasma in the ESRD patients.

So I guess the question is whether, you know, in terms of our criteria, whether we have evidence and if we don't really have evidence and if we don't really evidence then, you know, do we move forward under considering an exemption for the evidence or – what's your thinking about that?

Andrew Narva: This is Andy. I think lack of evidence that specifically takes plasma doesn't trouble me because I think we have a lot of similar examples where data was just collected certain way but it doesn't necessarily invalidate the use of the plasma.

I also think the fact that there's no NQF – when we considered this measure a couple of years ago we did not feel there was strong enough evidence to set a target. So, there's no target …

Karen Pace: Right.

Andrew Narva: … that we're endorsing. And mostly, the goal of this measure was really monitoring and be sure that there is awareness of this although there wasn't strong, really strong evidence of your target. It doesn't sound like specially in that light, very small differences don't have great implications here.

Jeffrey Berns: Can I ask maybe just a practical question that would help me decide and that is, when a lab is reporting one or the other and the call have been answered is I'm assuming that it will be clear on the lab report. This plasma (not) serum, did a lab change from serum to plasma if that's the case. And what the, you know, so called normal range is for that assay as opposed to a serum assay so

at least the practitioner will know what they're getting, I'm assuming. I just would like to have confirmation on that.

Karen Pace: And that's what I'm looking for. I think Andy sent me something about that he received from someone about (inaudible) coding and so that's a good question. Now, let's Greg and their lab folks weigh in and see if I can find this particular e-mail that I'm referring to.

Andrew Narva: I think there may be a different issue that I'm not sure.

Karen Pace: OK.

Andrew Narva: I don't …

Karen Pace: OK.

Lisa McGonigal: Are you asking whether or not the lab will indicate the normal parameters if plasma is done, I want to make sure I understood.

Jeffrey Berns: Yes, you know. So, that the practitioner knows that it's plasma not serum and you know, if they're so inclined can figure out or find out what the difference is and I'm assuming that the normal range would be reported.

I guess one thing we have to be, you know, aware of is if patients move back and forth, dialysis patients in particular, between deep different treatment settings. The hospitals and dialysis facilities so, you know, at one point in time, they're going to be getting a serum, another point, they're getting a phosphorous so it's important that practitioners know if there is in fact a difference and the patient may have two slightly difference, you know, very, very potentially …

Female: OK.

Jeffrey Berns: … slightly different results.

Female: Yes.

Greg Miller: This is Greg. I can comment a little bit of at least in my laboratory, which is in Academic Medical Center, we accept serum or plasma for phosphorus testing and we do not identify which type of sample was received when we issue the report form. So, the reference interval that's provided as a guide for interpretation does not – is not different whether it's a serum or a plasma sample.

Jeffrey Berns: And recalling, it's just phosphorus. I'm not identifying it any further, serum or …

Greg Miller: That is correct. The order is for phosphorus. The sample type is blood collected in either serum or plasma tube and the result is reported out in phosphorus, inorganic phosphorus without any indication what sample type was actually received.

Now, in a dialysis lab setting, I don't know how those labs operate, they may if in fact plasma becomes unacceptable sample type, they may choose to discriminate whether it was a serum or a plasma value.

Jeffrey Berns: There is a whole literature about albumin levels which aren't all that much different but they're just different enough to make people when they need to identify one or the other depending upon the assay, whatever that's worth.

Greg Miller: I think, in some of my earlier comments, the small differences when you do a study like of a hundred patients or some number of, you know, paired samples, you can identify these statically significant small differences or lack there of in the case of today that we saw in the ESRD patients a few minutes ago. But the small differences in sample type are much smaller than the differences in the patients, any given person's biological variability and actually probably smaller or as small as the differences in between laboratories.

So, if a patient is moving from one medical center to another, it's likely there will be enough of a difference in the actual method, value used that the small difference in sample type becomes unimportant and, you know, we're not good enough to really discriminate those small differences in making judgments about what to do for the patient based on the lab value.

Jeffrey Berns: That's helpful.

Karen Pace: Andy, I'm going to ask you whether this is relevant or not. What I was thinking of was a – I think it's along the lines of what Greg was just saying. It was from Clem McDonald.

Andrew Narva: Yes, all right, yes.

Karen Pace: OK. And it says from a lab experience, this laboratory test, serum and plasma testing provide equivalent or within patient equivalent results for almost all chemistry and most serologic tests. Increasingly because of processing convenience, plasma is preferred over serum.

Let's see. And he said in regards to phosphate measures in intravascular fluid, there is no distinction in this code. He's referring to the LOINC codes for serum and plasma.

Andrew Narva: That's right I did send you that. Yes, he's here at the NLM. He's the inventor of the LOINC code, which Greg probably knows more about than, I'm sure, about than I do.

And I think the point that Greg makes about (inaudible) variability and intra-lab variability is greater than the difference – than the range of potential difference between these two different assays is just – it sort of brings us back to Earth and suggest that kind of – you know, that we're actually almost demanding a level of certainty that may not exist and that may exceed what we look for another test.

Karen Pace: Right.

Jeffrey Berns: I'm inclined to agree at this point.

Karen Pace: OK. All right. Let's open up for public comments and then we'll come back to the panel in just a moment.

So, operator, do we have anyone on the public line?

Operator: You have no one on the public line.

Karen Pace: OK. Is there anyone else on this call that would like to make a comment for the panel to consider as they're thinking this through?

Male: Yes, sir – I mean, yes ma'am, it's (inaudible), you know. I just want to make – to support the statement that in our experience, most hospitals tend to use plasma as well and it's interchangeably used in ESRD patients when they go back to dialysis and in fact CMS allows that to put in hospital values and (inaudible) for calcium and phosphorous. And then they'd already used (plasma).

The other point so, on – in the ESRD lab, we only use serum and I think what's also important is as long as the trending is there and that you don't jump in one particular value. There's not going to be a big clinical risk and I end there, thank you.

Lisa McGonigal: Karen, I wanted to ask something to you. This is Lisa McGonigal. I just wanted to point out again that this is – the reason we requested is because that it has potential unintended consequences and the issue is primarily that it's not really reflecting the true care that's going on when this measure is included in the ESRD (clinics).

The values are being drawn by these labs that use plasma but it wouldn't be reflected and they would be penalized, indicating that weren't providing appropriate care when, in fact, they really were. So, that's one of the big issues that I didn't want people to lose sight out here as well, that the care is being provided appropriately but that there being – would be assessed somewhat inappropriately in this instance.

Karen Pace: OK, thank you. Any other comments from CMS or Joe?

Joe Messana: I have nothing to add beyond my initial comments related to peer-reviewed literature. Thank you.

Mary Pratt: Hi, Karen. This is Mary, I have no further comments. Thank you.

Karen Pace: OK. All right. So, let me come back to the panel then and see if those of you on the call are ready to make a recommendation. I know we have a few panel members that were unable to make this time when we had to change the time. And so I think what might be the best approach is to see if you all want to weigh in on the recommendation and then certainly, we can check with our other colleagues from the panel and summarize the discussion.

And certainly, they had all the materials just to see if they have a different perspective that we need to bring back to you but if – so I'm going to just ask if the panel is ready to weigh in on the recommendation.

Jeffrey Berns: I think I can.

Karen Pace: OK, Jeff, you want to start us off?

Jeffrey Berns: You know, I don't – I think this is OK. I don't have any objections.

Karen Pace: OK.

Andrew Narva: I also agree with that. I think it's OK.

Karen Pace: OK, and that's Andy, OK.

Debra Hain: Hi, this is Debbie, I also agree with it and especially from a clinician point of view, someone had mentioned, trending of labs. As a clinician, I always try in lab. So, it is of the change, the differences between plasma and serum. From what I can see, what available evidence we have is not that much to make that and so clinically, I don't see that it's going to impact my practice.

Karen Pace: OK. Thank you and Greg.

Greg Miller: I agree that serum and plasma should be able to both be used.

Karen Pace: OK.

Greg Miller: I'm not sure what I'm agreeing to.

Karen Pace: OK, that's very clear, thank you. All right.

OK. So what I will do is write up a brief summary of this and your preliminary recommendation and share it with the other members of our panels, just to make sure that we haven't left anything unturned in terms of, you know, perspective we may not have considered.

And then, our next step would be once I check in with those other panel members. Of course, if anything comes up from them, I would get back to the full panel and our CMS and KCP colleagues. But otherwise, we will be posting the recommendations for comments.

And Elisa, how long is that comment period or …

Elisa Munthali: Actually, that's 15 days, am I correct?

Karen Pace: Yes.

Elisa Munthali: Yes.

Karen Pace: OK, so we would have a 15-day comment period to more widely get some input into the discussion and hear from anyone that is an interested party and we would then share those comments, ask these expert panel but ultimately, all of that information will go to our consensus standards approval committee to make the final determination of how to proceed.

So, I think – unless there's any other questions or comments that someone wants to bring up, we can give you back a few minutes of time today but I'll just see if there's anything else or actually, if there's anything else from a process standpoint that we need to consider.

Elisa Munthali: No, that's it. We've covered anything.

Karen Pace: OK. Anything else from any of the panel members?

OK. All right. Well, thank you all for joining the call and your time in reviewing the materials and we will keep you posted on where we're at with things. Really appreciate it.

Female: Thanks. (Inaudible).

Male: Thank you.

Female: Bye-bye.

END