Roundtable Discussion
Facilitator: Dr. Winn-Deen

Before we begin the roundtable, let me first express my appreciation to Dr. Winn-Deen, Dr. Leonard, and Ms. Zellmer for agreeing to serve as facilitators of a roundtable discussion. Their role is to help amplify the oversight issues and focus our discussion, but all members and ex officios are also encouraged to please join in and raise questions and issues. We want to be sure that we cover all of the salient points. So, Dr. Winn-Deen, I'll let you take over now. Thank you.

DR. WINN-DEEN: So I guess what I'd like to do first is to ask if there are any specific questions that anyone on the committee has before we sort of kick off our discussion, or any of the ex officio people as well. Hunt?

DR. WILLARD: Just a question for clarification, at least for me and I suspect for some others as well. It is not clear to me to what extent your purview on genetic testing and the range of questions you're considering exactly parallels what you would do for, for example, in the case of a new imaging test that the radiology community was bringing forward, or whether you are truly considering genetic testing in a totally different light that brings in and raises questions that you'd never consider when MRIs came along or some new imaging technique came along. Depending on your answer, I may have a follow-up.

DR. BOONE: Well, I think you're raising what are sort of the horns of the dilemma that we've been facing all along, which is is there enough specificity in CLIA at present to deal with genetic testing, or do we need to add some specificity to encompass genetic testing? I don't think the answer is completely clear on that. I do think that it would be awkward, since we have no genetic heading/category under CLIA, for the rest of the world, if you want to take it from the world view, for us to have a major clinical laboratory oversight that doesn't have a specialty for genetics, just from the perspective of the public. They would expect something to be -- to have some specificity about genetics in a rule, I would think.

The other side of this that also is affected is the payment side. If you have some specific categories for genetics in a rule, then CMS has a little bit easier time of paying for those specific tests as well. So it's not just the black and white issues of whether or not there is something unique or exceptional about genetics, but it's also that you have to take into account the overall regulatory process and what effect that process has on a specialty area.

DR. WILLARD: Let me try to focus the question so that we don't get spread that thin. From the standpoint of CLIA -- or let me phrase it in terms of this new hypothetical imaging test -- would you just concern yourself with the analytical procedure of imaging or would you be equally concerned about the pre-analytical, the post-analytical, the equivalent of genetic counselors, how people would charge for it? Is that all within CLIA's purview for every test that's done on human subjects or on human patients?

MS. YOST: Right now, the umbrella oversight for CLIA is obviously the CLIA law, which is fairly broad. It certainly didn't anticipate the type of technology that's available today back in 1988, and so it doesn't really cull that out. However, because of the issues that came up with the notice of intent that Joe just articulated, we have actually asked general counsel from CMS to evaluate those issues to determine the extent of the authority of CLIA regarding those issues. So that is actually under review at this time, the clinical validity versus analytic validity, the informed consent, the counseling process.

What is the extent is actually where is that line, and it's not clear from the statute or from our reading, so we need to have attorneys review that and make a determination for us, and that will then help to determine the focus of that proposed rule.

DR. WILLARD: Let me ask one more focus question and then I'll be quiet. So informed consent is a great example. Does CLIA worry about informed consent for the other thousands of tests that you regulate?

MS. YOST: Not at this time. It does not.

DR. WILLARD: So what is the motivation for considering for the first time ever informed consent as being under the purview of CLIA when it's never been there before for the previous 10 or 15 years?

MS. YOST: I believe that the CLIAC had very good intentions and also felt that part of the pre-analytic phase of testing could include informed consent. So they made a recommendation that there at least be some connection within CLIA, not total oversight because clearly that resides elsewhere, but at least to be considered as Joe indicated, perhaps just a box on the laboratory requisition, which is covered under CLIA, that the informed consent was obtained and that there was documentation about why it was not.

But at this point, again, that issue is one of those that is with our attorneys under review at this time.

DR. WINN-DEEN: I think we'll take a question from Ed, and then Reed, and then Arden.

DR. McCABE: Ed McCabe, and please, if you could, state your name for the record.

I have two questions. One was raised. Joe, you mentioned about specimens crossing international boundaries, and my question is is there a responsibility of the individual who is ordering the test, the health care professional, if the specimen is being sent to Canada or to Europe, where there is no CLIA, if I'm ordering a test, what are my responsibilities toward that test?

MS. YOST: Any testing that's performed on specimens from U.S. patients or clients, the facility that provides it, regardless of its location in the world, must have a CLIA certificate. So it is the prerogative of a provider to order a test. However, when it's a U.S. patient, the facility that provides the testing, regardless of where it is, is required to have a CLIA certificate.

DR. McCABE: But in genetic disease, there are a lot of rare diseases, and there may be labs where there's only one lab or two labs and they're not in the U.S., and they aren't CLIA approved because they don't feel that they have adequate volume to seek CLIA approval. So then we should not be ordering those tests.

MS. YOST: No. The laboratory should have a CLIA certificate. I'm not going to say don't order the test. I'm going to say the laboratory needs to have a CLIA certificate.

DR. McCABE: But this is a problem for rare diseases.

MS. YOST: I realize it is a complex situation. We've dealt with it in the past, and I guess it's

really most important that individuals ordering their tests search out or seek out laboratories that could provide that service that have a CLIA certificate for their patients. I mean, we're talking about a safety issue here too.

DR. McCABE: But I'll just point out that I saw a patient with Hershbaum's disease a couple of years ago. The only laboratory that I could find that was offering clinical testing at that time was a laboratory in Canada, and as a result and because I was aware of this issue, we were unable to get testing for that family because there was no lab in the U.S. that was providing the testing. So it basically prevented that family from having testing from a reputable academic center. I mean, we just have to recognize there are issues.

MS. YOST: It's a double-edged sword. I mean, there's a quality issue on one side, and then there's an access issue on the other, and I think certainly we're willing to work to resolve that. I don't mean to take a hard line, but I need to tell you what the requirement is at this point. That's my responsibility.

DR. WINN-DEEN: Judy, can I take the chair's prerogative and just ask a follow-up question here? This is Emily Winn-Deen.

MS. YOST: Sure.

DR. WINN-DEEN: What are the barriers when you go out to these small research labs? What do they perceive are the barriers to getting a CLIA certificate so that they could offer that kind of testing for real patient service to anyone from anywhere in the world who might need it?

MS. YOST: There may be a couple, one of which is perception. It's an unfortunate thing that people think it's a big bureaucratic requirement to have to meet CLIA requirements when more or less they are very straightforward. They are implemented -- you know, I gave you the whole spiel this morning, so I won't go through it again. But people feel that it's a huge, huge monster to have to deal with, a paperwork nightmare, and it creates a lot of work, and it also requires a lot of personnel with specific qualifications that perhaps they don't have available at an additional cost. I think those are some of the major concerns that I hear. But part of it is really just not understanding how the program works and what its intent is and getting correct information.

We do our best to get the word out. We're hoping that this committee will assist in getting that word out so that people can understand that it's clearly not as complicated or difficult to meet CLIA as it may appear on the surface. If you get the federal regulations from 1992, it's 200 pages worth of requirements and you think, oh my God, I'll never do this; or you get the CAP checklist, which is hundreds of pages of questions, and that's not CLIA. CLIA is really the very simple things that I explained, and that's what it's intended to be, and then whatever somebody else makes of it obviously is different. But I think that's part of the difficulty, that folks understand.

The costs are relatively inexpensive only because we have very, very low fees that don't even cover our costs for the smaller laboratories, both for their inspection cost and their certificate. We intentionally kept those low because we realized that there would be not just small research labs but small doctors offices, small clinics where it would be prohibitive to be able to meet CLIA. The idea again is to help the laboratory be able to meet the requirements.

DR. WINN-DEEN: So could you just tell us if you were the lowest volume, anything out there, what's the bottom of the fee schedule?

MS. YOST: The bottom of the fee -- it sounds like the bottom of the whatever. But anyway, the lowest certificate fee is $150 every two years, and the lowest survey fee is $300 every two years. So that's $425 a year, and that's for up to 2,000 tests a year.

DR. WINN-DEEN: Thank you.
Reed?

DR. TUCKSON: Two related questions. Reed Tuckson, by the way, and thank you both for those excellent presentations.

Joe, I get the sense that this is going to be a while, and there's no question it's going to be a while, a long while. In the interim, based on Huntington's point, today people are doing things, there are tests going on today. I guess the question we need to be -- at least I need to be comfortable about is how comfortable are you today in assuring the American people that the testing for these diseases in normal medical practice today is adequate, that the public is protected in the interim while we wait for all these extra things to occur? How do we know the quality of the protection of the health of the American people in this area today?

DR. BOONE: Well, that's a very difficult question to try to answer, but we do have the New York State information, which if you want to look at the most heavily regulated area where they actually do look at the test validity of all the tests that are being done on New York State citizens, one of the actions that they've taken -- and about 50 percent, I believe, of the laboratories participate in the New York State oversight activity, so it's a fairly substantial part of the overall testing group that participates. They actually did withhold the ability of one laboratory to provide testing to New York State citizens. Because we don't have as much specificity in our law right now, I think that it could be a little bit problematic for us to go that far.

Then you've got the international community that's going to drive this as well. So I do think that there's a lot of concern that's being expressed. We don't have any hard evidence that real harm is being done, but we've got a lot of anecdotal kinds of information that would indicate that we could.

DR. TUCKSON: Well, Joe, let's do this. Maybe in the interest of time because we probably can't drill any deeper, and also I don't want to put you on the spot for this kind of question, but I think what I would appreciate as a supplemental set of material is if you are the head of the CDC or you are the head of the FDA, or you're the head of CMS, somebody somewhere must have a checklist that sort of says how do I know whether or not this system that is designed to protect the health of the public in this area, whether it works or not? Because clearly we've got rules that all these people are meeting because they're worried about making sure something doesn't go wrong. Great.

The question that I don't understand is what would be the checklist that they're looking at to determine whether all these zillions of regulators and all these people and everybody out there doing all this work, how do they know whether or not it's effective? I'm just curious what the criteria would be that everybody is using as a yardstick for whether or not this thing works or not.

The only other question I have is -- and I really appreciate you putting it up there as a question mark on your last slide, and I know probably that under the constraints of government you're unable to answer this. But do you all have the resources to do this job? Do you have the resources today under your present definition of CLIA, and then what will it mean going forward? Because I don't know how anybody will be able to evaluate the budgets that are

submitted by HHS in this area to know whether or not they're adequate or not, and how important it is in terms of your resources.

So I don't know the way we begin to look at that, but again our job, as I understand it, is to begin asking these questions and thinking about protecting the public in this regard. So I just don't know what criteria we can take from your presentation to know whether or not you've got the resources.

DR. WINN-DEEN: I think Muin is going to answer you, behind you, from CDC.

DR. KHOURY: This is Muin Khoury from the CDC. Reed Tuckson always asks the right questions. I've known that for a while now. He asks questions that have no immediate answers, unfortunately.

If you all recall back from the discussions during the SACGT years when we discussed the issues of oversight of genetic testing, the previous committee recommended essentially a three-legged approach to the issue of genetic testing. One is an FDA approach. The other is a CLIA approach. The third one is essentially a non-regulatory approach to try to collect data on what's going on in the real world. So based on those discussions we had in the previous committees, and also the essentially non-regulatory nature of CDC as an entity, we began developing approaches to deal with those issues that Reed is asking about, what's going on in the real world.

Unfortunately, with the issues of resources that are not coming to bear on genetics per se at CDC, and some of the barriers that Joe mentioned, it's very hard to collect that kind of data in the real world, but we've made some progress. I think what's going to happen based on the discussion of this committee, we're willing to give you a more detailed briefing on the non-regulatory approaches that CDC and also other agencies have been engaged with to try to collect data on the full range of parameters of genetic testing, from the analytic performance in the lab all the way to the clinical utility and the ethical issues in the community, as well as utilization rates.

But we don't have answers to what you're asking, Reed, but we have begun developing approaches to try to come up with those answers in the long run, and these approaches are also equally difficult and they would take time to implement. But we'll be happy to give this committee a fuller briefing next time.

DR. WINN-DEEN: Arden Bement?

DR. BEMENT: Arden Bement, Department of Commerce.

My question is to Judy Yost. On your slide 6, under your quality standards and under proficiency testing, you require an external test for accuracy for a private organization. Is this private organization certified? Is there a chain of conformity in the program?

MS. YOST: Yes. There are specific regulatory requirements that the private organizations need to meet, and they actually go through a wonderful annual approval so they can provide this testing by CMS.

Since you brought that up -- I thank you, actually -- there is an answer to Reed's question. There is one small measure, actually, that CMS has in place already. If you recall, I said that with laboratory testing it's a little bit different in many cases because you don't have a patient. It's one step removed from a patient. You have a provider ordering a test, the test result going back to

that provider, and it's the provider who takes the action with the patient. So we don't have a lot of outcome information. If you remember, I said the test result is the outcome that CLIA is authorized to measure under its analytical purview.

However, there is one measure that we have, and that is the proficiency testing, because that data is collected and maintained and evaluated, and we use that data currently. Again, it's not for where there is not an organization that provides this on a regular basis to the laboratory, so that a lot of genetic testing isn't measured by this process. But for those tests that are, and there are about 84 different representative analytes under CLIA that do have structured proficiency testing, we actually look at that data to look at laboratories' performance on an ongoing basis to determine, number one, are they enrolled in proficiency testing correctly and are they performing appropriately under proficiency testing.

So there is one measure that we have maintained over the last five years, actually, to evaluate laboratories' performance, because proficiency testing is well documented in the laboratory community as a measure of accuracy of testing. It's a long-term measure of the accuracy of the laboratory's testing. So we have been monitoring that over time, and I am also pleased to tell you that from the data that we have collected, something that almost pulled the entire CMS data system down, it's that much data, because if you realize proficiency testing is five specimens three times a year to every laboratory for each test that they perform that's regulated, so it's a huge amount of raw data that has to be compiled and synthesized into these reports, and we are looking at about a 98 percent threshold whereby every laboratory that's supposed to be enrolled is enrolled; and secondly, laboratories' performance has improved significantly since CLIA began in 1993, and we actually began measuring this more in 1995 when we had our act together a little bit better, until the present.

So that information is available and it is made public actually every year. It's called a Government Performance Review Act that was passed by Congress.

Thank you.

DR. WINN-DEEN: We'll take one more question from Deb Leonard before the morning coffee break.

DR. LEONARD: Debra Leonard. I actually have two quick questions, one quick. Can CLIA create relationships with other quality monitoring programs internationally, and are you working to do that? Because I'm sure the laboratory in Canada was monitored by some program if it was a clinical laboratory.

MS. YOST: Yes, very much so, and actually we are in the process of working with that now, because we do have a number of foreign laboratories already enrolled in the CLIA program in our database. Most of those are actually accredited already by a private organization, so basically we've assumed that they're fine. We are going to set up a more formal process, however, but we have not determined exactly what route we will take for that. We're looking at various options, one of which is an agreement with a private organization.

The other is to use the -- there is an international laboratory quality standard that was recently published, I believe it was last year. It's an ISO standard that is cross-referenced to the ISO 9000 documents. It's one specific for laboratory medicine, and we may use that standard as a possibility whereby if a country would adopt that standard as its national regulation or quality standards, that we would accept that as equivalent to CLIA. So we are working in that direction

as we speak, yes, and that might help some of this international problem, because a lot of countries, at least 30, have indicated, that I'm aware of, that they will adopt that standard as their national requirements.

DR. LEONARD: The second question is how many problems, even anecdotal, are with CLIA labs as opposed to those laboratories that are not trying to meet the CLIA standards, and what mechanisms are there for identifying those laboratories and bringing them under some sort of regulatory process?

MS. YOST: I'll start and Joe can finish. We have certainly seen -- I think all of us have some great horrible horror stories anecdotally of problems that are not necessarily documented of laboratories that do not understand the importance of doing some sort of routine check on a daily basis that their testing is working, that they have not evaluated the validity of the types of testing that they're doing, the accuracy, the precision and so forth; or they have not reported the tests in a timely fashion where it's useful to any kind of caregiver.

So we have a number of pieces of information like that. Obviously, data from our surveys from those that we do overseas, we've got plenty of background information on those laboratories. But for those that have not, when we find them, we have found some fairly significant problems in labs that do not have oversight because they just may not be aware of the importance of meeting some basic quality standards.

As far as efforts, we don't have a formal program, partly because of resources I guess, to go out and beat bushes and really to do some sort of ground-level encouragement of people to come into the program. We certainly have a plan in place to talk about how we might accomplish that, by working with entities that we typically do not, such as university organizations and genetic testing symposia and those sorts of things, where the folks who might be the ones we're looking for might be attending so that we can do this in a very non-threatening way to folks, because it's very important that they understand that there is no penalty. If you're not enrolled, we give you the benefit of the doubt one time around. Everybody is given that allowance.

So again, I have a plan written. It's just because of resources and being overtaken by other priorities that I've not been able to follow it through.

DR. LEONARD: So you seem to be confirming -- are the egregious problems that you're talking about, were those in CLIA labs or non-CLIA labs that then when you went into there were problems and they got identified, and they got corrected --

MS. YOST: And they got corrected. It's both.

DR. LEONARD: -- through the CLIA process?

MS. YOST: Yes, yes. It's both, actually. There are many that are doing just fine. I mean, some of the initial laboratories that we visited that were doing specific genetic testing research actually had done so much work in the preparation of the test that they had developed that they had gone well beyond what CLIA would have required to meet QC, PT, and QA. So we were very happy with that.

Then there are other places that do not recognize, as I indicated, the importance of just doing some very simple things just to check on the accuracy of their testing. It was just a little less careful. So in those cases, then, we have serious concerns. But we have always said that CLIA is

an incremental process. You start out with the very basic, simple things. You make sure you have qualified people, you make sure they do some quality control, and over time they then recognize the importance of having some overall systems process in place to ensure accuracy.

So that's basically how it works. You start out with problems, but you find over time that we've helped people improve.

Have I answered what you're asking?

DR. LEONARD: I guess my question is are we regulating more stringently where we're already regulating and not doing anything to capture the problem areas, the problem laboratories?

MS. YOST: Well, we do focus our resources. What we do, as I indicated, our process is intended to visit people routinely. But for those folks who are doing a good job, it's kind of hi, how are you, and checking --

DR. LEONARD: But those are the CLIA labs.

MS. YOST: Right, those are the CLIA labs. For those that are not, if we don't know where they are --

DR. LEONARD: You can't get them.

MS. YOST: -- we can't get them, because we'd have no way of finding them. Oftentimes we have the old report on your neighbor -- "If I have to do this, so do you" -- and we get some of that. But we don't have at this point the resources to go out and dig up where there might be places where folks are unregulated that might need a hand in meeting the requirements.

Go ahead, Joe. I'll stop.

DR. BOONE: Well, I think there are two areas that this committee needs to consider. It's not just the regulatory agencies that have responsibility here. It's a societal concern, and so we need to be aware of what the professional organizations are doing and what their commitment is to identify the fringe areas, because that's really what you're pointing at. I think most of the problems that you're talking about and that this committee has talked about and that CLIAC has talked about are in the fringe areas, direct access testing kinds of concerns, laboratories without validated tests that are being offered.

Those kinds of things don't occur within the College of American Pathologists programs, and they don't occur to a wide extent, at least as far as we can tell, within the CLIA-certified laboratories. It's the group that's not under that umbrella that we're concerned about. I think the most aggressive, if you want to look at it from a regulatory standpoint, the most aggressive program is the New York State program. They would also point out that they don't encompass everything that happens in that state or to residents of that state.

So the outreach of the regulatory effort can only go so far, and we are only looking at minimal requirements. We're not looking at the level of requirements and expectations that a professional organization would look at. So I think it's very legitimate for them to set higher standards and to have those adhered to, but I don't think you should expect the federal government to take care of every problem.

DR. TUCKSON: What's the answer to Ed's question? I'm sorry to break in. But let's say that it wasn't Canada that he went to to try to get his test, but it was in Wyoming, and let's say he knew that lab didn't have a CLIA certification for that test. Would it have been illegal for him to have still ordered the test and used it, even if there's no exchange of insurance money and all that? It's just you and the patient who are doing this deal, the patient is getting the test and paying for it themselves. Is it illegal for him to do that? Is it unethical for him to do that? Is he required as a physician or an academic center to report that he is aware of this lab doing this that isn't CLIA certified?

MS. YOST: The ultimate responsibility under CLIA resides in the laboratory, with the laboratory where the test is performed. That's how CLIA operates. So I won't qualify what Dr. McCabe is, but I will say that it is his responsibility as a physician to report it to somebody. You can do that completely anonymously. I mean, you can just make a phone call to the state agency, to us, to our regional office and just let them know that, oh, by the way, I'm trying to get this test done, but I noticed that this laboratory doesn't appear to -- I mean, I think it's every citizen's responsibility, whether you're a patient or a physician, if you're going to have a test done on yourself or on your patients, that you should ask do you have a certificate.

I think that's the first and foremost question. That's what we teach folks who are looking for laboratory services. That's the first question. That's what Medicaid does to any laboratory that's going to bill them for any kind of testing anywhere. The first thing they want is not only tell me your number but send me a copy of that piece of paper that shows that you're certified, and not only are you certified but it's effective and that it's for the type of testing that I'm going to have done here. That's a very simple, baseline ground rule to use when selecting a laboratory for services.

DR. McCABE: Thank you very much. Thank you, Emily, for facilitating that, and thank you to Judy and Joe for your presentations and for answering our questions.

We'll now take a 10-minute break. We will shorten it from 15 minutes to 10 minutes. For the SACGHS members and presenters, there are refreshments here. For the ex officio members and members of the public, refreshments and beverages are available in the Starbucks Expresso Bar, the hotel gift shop, and the eateries at the Metro level. Please be back in 10 minutes. Thank you.

(Recess.)