Update on the Notice of Proposed Rule Making on a Genetic Specialty for the CLIA Program
Judith A. Yost, M.A., M.T.

MS. YOST: Good morning, everyone. How is everybody on this dreary day?

(Slide.)

I want to thank the committee for the invitation to meet with you today and also for Sarah and her staff for accommodating my horrendous scheduling and allowing me to be here this morning.

Since it's early in the morning and I only have a short period of time, we're going to fast forward on this presentation and move to what would be, I believe, your slide 14. It's going to say "Current Status of Genetic Testing Under CLIA."

We're going to assume that you know everything there is to know about the current CLIA requirements that include quality control standards as well as requirements for analytic validity. It also includes quality assurance requirements, requirement standards for proficiency testing, personnel qualifications and responsibilities with the lab director having the overall responsibility, recordkeeping requirements, and labs are inspected biannually. So that's our starting point for this morning which, of course, heads you to the first bullet that says, "Genetic testing is already covered by CLIA regulations under those standards."

In addition, there are specific standards already in CLIA for cytogenetics. There are quality control requirements as well as personnel qualifications and responsibilities.

There is, however, no genetic or molecular testing specialty currently under the CLIA requirements. The tests that you may want to call genetic tests are currently dispersed throughout other laboratory specialties such as hematology, microbiology, immunology, chemistry, even blood banking, I guess, if you want to go to that extreme.

We did, however, make some changes based on CLIAC. The CLIAC is the Clinical Laboratory Improvement Advisory Committee. They had made a series of recommendations to the Department of Health and Human Services regarding CLIA changes for genetic testing and we were able to, when we published our final quality control regulations, incorporate some of those recommendations.

One is a unidirectional workflow for PCR testing, quality control for PCR testing. We enhanced the confidentiality requirements in those regulations as well.

(Slide.)

Just as a little bit of history because you can't do anything without the background and history, there was a Department of Energy-NIH Task Force that published a report indicating that there should be enhanced oversight for genetic tests. That was in 1997.

In 1998, the CLIA Advisory Committee did make specific recommendations to the Department regarding what should be added to the CLIA requirements to cover genetic testing.

Then in 1999, your predecessor committee, the SACGT, made recommendations to support those CLIAC recommendations.

So in 2000, May of 2000, CDC published what's called a "Notice of Intent", NOI, and that really is like a predecessor to a proposed rule. It just says, "We're thinking about doing a rule and here's what it may contain." Essentially that that notice of intent included were all of the CLIAC recommendations as well as a comparison to what existing comparable requirements already were included in the current CLIA requirements.

That notice of intent did receive quite significant comments. Interestingly enough, however, the comments were very balanced. They landed on both sides of the fence on a total continuum from a position that said, "Well, maybe we already do cover genetic testing in CLIA so maybe we don't need to do anything" all the way to the other extreme, which was "very prescriptive, very detailed requirements belong in CLIA for genetic testing."

Based on that Notice of Intent, the CLIA Advisory Committee updated and revised their recommendations. I believe you have those recommendations as part of your package today in case you would like to look at them.

Currently, I am pleased to say that based on all those recommendations, we do have a notice of proposed rule making in CMS clearance at this time.

Now I'm sure you're looking at that timeframe and saying, okay, what have you been doing since 2001 till the present since there is, as you can see, a noticeable gap in time. You're probably wondering what we've been doing. Well, quite a bit actually. I think it's important that we owe—and we do owe you an explanation regarding that.

One of the things that was so difficult was the fact that those notice of intent comments were very mixed so it's awfully hard to write something when you have comments that kind of can go either way. It's kind of hard to frame and craft language that accommodates those comments. That was one issue.

In addition, some of the recommendations made by the CLIA Advisory Committee were actually outside the scope of authority of CLIA. So that also gave us problems in dealing with that. What, in fact, do you do when we don't have authority for certain areas? We don't have authority under CLIA to require, for example, informed consent. We don't have authority to cover clinical or utility or validity. So those were difficult issues that we also had to deal with.

In 2003, as you noticed from my previous slide, we published a final quality control regulation and that one was actually even later than this one. Unfortunately, we have requirements published back in 1992 that had been extended four times until 2003 and we felt we really needed to finish those first. That was the priority for the CLIA program.

Well, for those of you who don't realize, when you publish a regulation you're not done. That's the beginning. You've got to educate your surveyors. You've got to get that information out to the laboratories so they know what the standards are in order to be able to meet them. So CMS is the implementing agency for CLIA and thereby we had to train our surveyors and provide education to the public in order to meet those requirements, and then we could take up the regulation for genetic testing.

One other issue that also came to play here was the fact that again CMS does not have authority for clinical utility or validity. For that reason, there was kind of a hole in the process because, as you know, one of the more difficult or complex issues is how do you get a brand new test from the laboratory or the garage or wherever it is invented out to the marketplace and ensure that the

test, in fact, does what it says it does? So we were sort—there were a number of recommendations that had come forward from this committee and other groups regarding how that should take place and then CLIA would basically pick up the pace and take it forward into the analytical piece to ensure quality testing on a day-to-day basis.

Unfortunately, that part has never taken place and so it kind of left us with a difficult position of not knowing exactly where CLIA should start and end because there was this other responsibility that has not been done, not through anyone's fault but because there just wasn't the wherewithal to do so. So there were a number of issues that did intercede, which obviously took quite a while to address and so finally we do have this regulation in clearance at CMS.

(Slide.)

Now nothing is ever simple and nothing comes without issues. So these are the kinds of things that we'll be asking you as a committee, your colleagues in the genetic testing community, and the clinical laboratory community to be addressing:

What, in fact, should the definition—because this is a proposed rule so we are looking for your comments, you are the experts in the field, we'd like to hear from you what should the scope of that definition be for a genetic test?

How shall we handle informed consent?

What about the clinical validity piece? Where does it fit? How does it fit?

Proficiency testing is an issue because you know there is not a plethora of genetic testing materials just laying around waiting to be—particularly for rare diseases—waiting to be used for PT. So how would you deal with that?

Also, personnel qualifications. We clearly do not want to disenfranchise anybody who is already in the field. So how do you create the balance to ensure quality testing but not put people out of their jobs?

And then the old faithful research labs that are currently doing what they call is research but they are reporting results back so they do belong under CLIA.

So you can see that there are a number of issues that we'll be looking to you for comments because when you comment to a proposed rule we have to consider each and every one of those before writing the final rule.

(Slide.)

We've had a lot of input, a lot of excellent input from all of you and from our own advisory committee. We had comments from the notice of intent. We reviewed different professional standards and guidelines and the crediting organizations' requirements. We talked to subject matter experts and, of course, the other federal agencies in order to come up with—and I do want to thank CDC since Bin is on the phone for their invaluable assistance in drafting this proposed rule. The reason that it's at CMS is that all the CLIA regulations are published through CMS.

(Slide.)

Just for those of you who are not familiar with regulatory terms, there are actually more than just standards when you do a proposed rule. There is the preamble because that's where you're going to hear what is the rationale for why we did or did not do something, and that's where we're going to include the questions to the public for comments.

Then there are the standards. They actually constitute the smallest part of a proposed rule.

And then we need to talk about the impact. What are the costs of meeting these new standards? What are the benefits that will balance out those new standards, as well as the information collection?

(Slide.)

So, okay, where do we go from here? The regulation is on the CMS regulation schedule. I cannot promise you once it's out of our division and into clearance—we're going to do our very best to get it through the system but we cannot promise you a date at this point in time. It's just too early to tell. It has got to go through CDC, FDA and CMS and NIH clearance before it will see the light of day, and then be signed by the Secretary.

Once it's published, we'll probably have a 60 to 90 day comment period. We'll compile and synthesize those comments into a final regulation and ultimately then train our surveyors. Again, we'll be looking to you to help with those kinds of things with ideas for that as well as to develop any guidance and educational materials to facilitate laboratory compliance.

(Slide.)

And last but not least, if you're interested in any further information about CLIA, I encourage you to visit our website. It has got everything you ever wanted to know or needed to know about CLIA and I do thank you for your time. I'll be happy to take some questions. You can always e-mail me or call me. That's our office number.

DR. TUCKSON: Judy, thank you.

Dr. Chen, did you have any comments that you wanted to make at all on this?

DR. B. CHEN: No, I think Judy provided all the details that I think are very helpful for this audience.

Q & A

DR. TUCKSON: Well, thank you.

Judy, let me just ask as a first question here—first of all, thank you for the presentation and we appreciate it.

So let's make sure that we've got it all straight. I think we're going to need—my question is going to wind up being a request for some supplementary material from your office.

At the end of the day there is a very important oversight regulatory function obviously by CLIA in monitoring the appropriateness of laboratory services in this special area that we are concerned about.

What you are describing is that there are—if you look at the overarching public goal of what ought to occur in the public's interest to give it confidence and assurance that appropriate monitoring of these laboratory tests is being done that there are some gaps. There are some things that exist that are very good. There are some things that are—there are some holes. There are some deficiencies. You're describing then a process, if I understand you, by which those deficiencies are now being addressed in a methodical and logical way, and that you're saying that we, as a committee, may well want to follow progress there and maybe even have some input and maybe ask for the opportunity to comment here and there on some of these things as they go forward.

The first question would be timescale again. Is there an expected date by which there should be a conclusion to this stage of the process?

MS. YOST: Again, I can't commit to any date because I can't promise anything but, if all the stars align and everything comes together, we could possibly see something early in 2007 calendar year but again that's—there are a lot of places it has to go--

DR. TUCKSON: Sure.

MS. YOST: --after it leaves our office.

DR. TUCKSON: And so just—again, giving you every possible latitude of not being put in any position to guarantee dates and that kind of thing, as we try to look at the work of the committee in our next meeting, if you're talking 2000—early 2007, and we're now June-July of 2006—is there a point time where our input would be helpful to you? Is that input helpful to you in November, December? How can we—when is the time period for us?

MS. YOST: Well, maybe two places. One is that once it maybe reaches those final steps to help us get it over the edge and out to the public. And the other is really once the proposed rule is published, we would really value your input on approaches to inspecting the laboratories, any kind of educational materials that might be helpful to laboratories to meet the standards. Those kinds of things would be wonderful to have from you folks.

DR. TUCKSON: Lastly, and I'll see whether my colleagues have any other quick question, I would like—if it is possible—for two things to occur. First, could we circulate to this committee the summary work that our predecessor committee, the SACGT committee did, on this whole issue of CLIA oversight and these issues so that we will have that as sort of a background for how committees like our's sort of look at this?

MS. YOST: Mm-hum.

DR. TUCKSON: That's possible?

MS. YOST: Yes.

DR. TUCKSON: Secondly, Judy, could you give us a document—a succinct document that says here is what people like you view as the scope of what needs to be done in terms of assuring this appropriate oversight? What's in place today so you've got building block A, B, C, D, E. Then define the things that are not adequate and the things that have fallen through the cracks through no one's fault, FGHLM, whatever—I can't count—that was a mixed metaphor. So the things that

are missing and then that will help, I think, all of us to sort of focus in on what it is that we sort of need to be commenting on. Is that possible we could get that?

MS. YOST: Well, actually if you look at the slides that you have there, there is a listing of the existing CLIA requirements.

DR. TUCKSON: Okay.

MS. YOST: I mean a very concise listing but in the earlier part of my presentation on one of the slides it talks about—it starts with personnel qualifications, I think.

DR. TUCKSON: Okay.

MS. YOST: It walks through what's already in existence. Not in great detail but at least to provide an overview.

DR. LEONARD: If you look at Joe Boone's slides--

DR. TUCKSON: Right.

DR. LEONARD: --it's in there.

DR. TUCKSON: Deborah is reminding us that in Joe Boone's it is there as well. Emily, did you have a comment?

DR. WINN-DEEN: I just wanted to ask what the opportunity is for revving the regulations to take into account changes in technology, changes in the field? It has obviously been quite a number of years since the original recommendations were drafted and a lot of things have changed in the world of genetic testing and a lot of things are still the same but there's a lot of changes that have been happened. What's the process for continuing to keep them updated?

MS. YOST: That is a wonderful question because one of the difficulties we had was that it was a moving target as time progressed and it is a revolutionary field. Everything was changing so it was our belief that if we wrote probably broader requirements in the regulation that we could have more detailed information in what we call our guidance document because that's more easy to change. We clearly did not want to have something out on the street that was outdated before it ever made a final rule. So instead we were looking for broader guidance in the regulation and then by policy and interpretation provide the specific guidance to the laboratories and to the surveyors.

We develop our guidance document with a dual role. Our guidance document is number one for our own surveyors to use to assess quality in the laboratory but now we write the guidance documents—since 2004, we have been writing that document to also include information to help the lab meet the requirements and also to know what the surveyor is going to be looking at. So it serves a dual purpose and that's where I would see--and we can update that routinely. Whereby a regulation, as you know—I don't have to tell you—takes a long time to get out on the street.

DR. TUCKSON: Right.

MS. YOST: So that was—that's our thought process behind that.

DR. TUCKSON: Judy, I want to thank you very much. What we'll do is this: I'm going to take Debra's lead on this and what I'm going to ask is Sarah and the team, we're going to put together for you, based on Dr. Boone's slides, also Judy's slides, and the stuff that we did in the predecessor SACGT committee on this, a little sort of focusing document for the committee to sort of look at so that you—so that especially again—again I'm going to be like a broken record on this, especially for the newcomers so that you really get a sense of where this thing is.

I think what we'll do is we'll put that together so we'll have it in front of us and then the committee can decide based on our priority slide, which oversight is on that set of priorities, is where do we see the importance. And we will decide whether we really—how much—I think we're going to—we have to respond to Judy's request when she sends us stuff but we'll decide how much energy and how best to attend to this important issue as we go forward in the next meeting.

So with that, Sarah, we'll put together something and we'll get it out to the committee in the interim between the meetings and we'll take a good look at it.

Judy, we are looking forward to however we can be of help to you and thanks again for joining us.

MS. YOST: Thank you.

DR. TUCKSON: All right. Take care.

Let me note with very great pleasure that we have been joined by Dr. Janet Woodcock, Deputy Commissioner of Operations at the FDA. We're honored to have her with us this morning and we'll be hearing more from her a little later about the Critical Path Initiative as it relates to pharmacogenomics and so we'll be hearing some things there. In addition, she has kindly agreed to stay for some of our discussion. I know her schedule has got to be probably be very fluid but she is certainly—however long that she can be with us is terrific.

Janet, we sort of talked earlier before you arrived about the priority that this committee has to get stuff done and we are very, very appreciative of having senior leadership from around the—from HHS to be with us and to make sure that you help us to get things done. So welcome and thank you for joining us.

DR. WOODCOCK: Thank you.

DR. TUCKSON: Great. Let me reset the thermostat and look at the meeting agenda again so you can know what's coming and where we're trying—what we're trying to achieve for this meeting.

For most of today we return to our work on pharmacogenomics focusing again on the development of recommendations that we'll be making in our report to the Secretary on this topic. As part of this discuss there will be the comments that I mentioned from Dr. Woodcock.

This afternoon we'll be updated about our draft report on the policy issues associated with undertaking a large U.S. population cohort project on genes, environment and disease, which is currently undergoing public review and comment, and learn more about the environmental components of gene-environment studies from two national experts in this field.

Tomorrow we will pick up with our deliberations on gene patents and access, which we began in March. Debra Leonard and our task force on this topic have organized a session that will provide a framework for the decision that we need to make on this issue, namely whether we need to take further action on the concerns and questions we identified in 2004 about the clinical care impact of patents. So again just to focus you in, we have had a very long discussion, a very good discussion led by our subcommittee team on this issue of genes and patents, and now to focus in as you look at all the things that you could look at on that topic, we really see a need to look at the clinical issues associated with it and that's what we're going to have a very focused discussion on tomorrow.

Tomorrow afternoon we will hear about the progress that some key stakeholders have made in advancing the prospects for advancing of pending legislation to prohibit genetic discrimination in health insurance an employment. We'll also be updated by FTC, FDA and CDC about their working groups on direct to consumer as I mentioned in my opening comments.

Public comment sessions are, of course, scheduled for both days. Individuals who would like to provide testimony and have not already signed up should do so at the registration desk.

Now let me turn to Sarah to do the policewoman 101 function about the ethics rules, which she's very good at.

MS. CARR: I am going to be very brief. You all remember that before every meeting your financial interests are reviewed and we try to make sure that there are no topics that come up no the committee's agenda that might pose a conflict for you. So we always rely on you, though, at every meeting to be attentive to your interests and to make sure that something specific doesn't come up that might pose a bit of a problem. If it does, we ask you to recuse yourself.

Also, as you know, we're advisory to the Secretary of Health and Human Services. We don't advise the congress and as special government employees, which you are when you're here for meetings, you also may not lobby the congress. So just be careful not to do that while you're here.

DR. TUCKSON: We've got our eye on you, folks.

MS. CARR: And that's it. That's it. We thank you for being so careful about all these rules.

DR. TUCKSON: All right. Thank you.

With that, are we cool or do I need to tap dance?

DR. WINN-DEEN: We're just about there.

DR. TUCKSON: I think that means I'm supposed to tap dance for another second.

(Laughter.)

Let me just ask the committee, by the way, are there any questions that you have? Are you comfortable? Is the committee—do you understand what we're about to try to do? Are you okay with the direction? Are you feeling like you're locked and loaded on what we're trying to achieve? All right.

Well, with that, we are particularly pleased that Emily Winn-Deen continues to be our leader in the pharmacogenomics, and to give us an overview of update and efforts on our pharmacogenomics task force.

Thank you to all the members.

By the way, those of you that are again new, you will—if you have not already—have the chance—will be wonderfully participatory in a subcommittee and, oh, will you be so happy that you did.