Public Comments

DR. TUCKSON: Let me invite Deborah Kloos, Gentris Corporation. We appreciate the public testimony and we love you to death. You know, by the way, the draconian five-minute rule.

MS. KLOOS: No.

DR. TUCKSON: Did they tell you that? Did they tell you what happens if you go over five minutes?

MS. KLOOS: No.

DR. TUCKSON: Well, you don't want to know.

So we appreciate the public testimony and we're really happy that you have come forward to us. And thank you.

MS. KLOOS: Good morning, Dr. Tuckson, and members of the committee. I do represent Gentris Corporation, a pharmacogenomics company located in Research Triangle Park, North Carolina. As one of only a few manufacturers currently focused on the emerging pharmacogenomics industry, Gentris manufactures products for predictive genetic testing, including reference controls and in vitro diagnostics.

From the beginning, we have been directed by the FDA to achieve clearance on all of our products. Such a process is not entered into lightly, since cleared products must demonstrate documented design control from the conceptual stage to manufacturing while complying with good manufacturing practices. However, we agree with the FDA that this is the best way to ensure that consistently reproducible reference controls obtained from properly consented patients are readily available to meet CLIA testing requirements. We have met these challenges and received clearance in December 2006 for six human genomic DNA reference controls for testing of the P450 CYP2D6 gene.

Gentris chose reference controls for our first 510(k) product submission based on the fact that there was one FDA-cleared platform for CYP2D6 testing, the Roche AmpliChip; CYP450 test. CLIA requires that laboratories use controls when performing genetic testing in order to ensure accurate results. We agreed with the FDA that it would be very helpful to the genetic testing industry to provide reliable, cleared companion controls for this cleared platform. Our concern is that this committee might be unaware that non-compliant material from other sources is also being used for the same purpose. This discrepancy is very disturbing to many in the pharmacogenomics arena and calls for action on the part of those in a position to effect change.

Currently there are three main resources for labs wishing to obtain genetic testing controls: one, leftover patient specimens, with or without direct informed consent; two, commercially available research use only or research-grade products, obtained most notably from the Coriell Institute for Medical Research; and three, FDA-cleared in vitro diagnostic controls manufactured by companies like Gentris Corporation and also Maine Molecular Quality Controls, Incorporated.

There are drastic differences between types of resources. Materials sold as RUO are not required to be manufactured under GMP regulations, so they have virtually no regulated quality assurance requirements and are not subject to FDA audits. Their performance characteristics have not been established; neither are they to be used for diagnostic procedures.

In sharp contrast, a small company such as Gentris dedicates large resources of time, money, and personnel to perform clinical trials, submit products for FDA clearance, maintain stability data, and manufacture products in a GMP environment. However, we believe it is well worthwhile to produce products that are qualified for use in diagnostic procedures. We can find no justification for lowering the bar for reference controls when they are such an indispensable component of pharmacogenomic testing.

It is evident that a great deal of attention was focused by CAP, CLIA, and CLSI on providing rigorous guidelines for genetic testing since up until now, only RUO product and residual patient material were available to laboratories. We were grateful to have had a source like Coriell for research-grade reference control material. However, now labs do have other alternatives for many controls as companies like ours are ready and willing to take the baton and meet the higher standard of producing IVD controls. Unfortunately, we continue to see research-grade products or leftover patient samples being put into clinical practice without the safeguards required for IVDs. As long as labs are permitted to use these, they have no incentive to use any FDA-cleared product control. This disparity needs to be resolved before companies lose their incentive for manufacturing IVD controls. It is unreasonable to expect the manufacturer to produce a regulated product when alternatives are still available at a lower cost because they are essentially research-grade products.

So what are we asking of you, the committee? The regulatory infrastructure has not caught up with the state-of-the-art technology. The result of this is confusion regarding what the rules actually are and a failure to apply the rules evenly for all. We urge the committee to recommend to the Secretary of Health and Human Services that its office seek congressional legislation or some other means that would create parity for manufacturers and harmonize the oversight of this area of genetic testing.

We know that the FDA is doing its best to enforce the ASR rule to ensure that only FDA-cleared products are used in situation where there are life-threatening consequences. But we also know that they are seriously underfunded. We're asking the committee again to recommend to the Secretary that his office seek increased FDA funding for the oversight of this particular issue.

This committee can play a key role in assuring that the health care community has access to the highest possible level of genetic testing controls and assays. Thank you for the opportunity to bring this to your attention.

DR. TUCKSON: Deborah, first of all, is it Dr. or Ms.?

MS. KLOOS: Just Ms.

DR. TUCKSON: No, it's not just. You'll now get me in trouble.

This is terrific. Are you going to be around this afternoon, or are you going back?

MS. KLOOS: I have a flight this afternoon, but I'll be around for a little while.

DR. TUCKSON: First of all, this is very important, what you have said. The one thing that at least gets my attention -- I don't know about others -- is the committee often, I think, has to be legitimately concerned about the private sector saying that regulations stifle innovation. So you'll say, well, you know, you guys who don't run companies, you don't know that when you talk about more regulations, more regulations, what you do to stifling innovation. Now, here you are saying

we run a company and there needs to be better regulation. So it's not an either/or, black/white deal.

MS. KLOOS: Exactly. What we were saying is that we were presented with a need. We've met that need, and now what we're seeing is laboratories unable or unwilling to use IVD-cleared product because they can get something else cheaper and it's not regulated.

DR. TUCKSON: Here's what I'd like to do. We're not going to be able to, as you heard from the last discussion, jump straight to legislation. The timing of your presentation couldn't have been better.

Would you be available -- outside of the meeting process, if you could provide specificity, as you've done in your testimony. One of the things that we were asked to do is find areas of harm or a threat of harm, and you have very granular knowledge here about an area. If you could provide that to the staff so that the committee can start to examine that, you will have gone a long way in advancing the committee's work.

MS. KLOOS: I'll be happy to.

DR. TUCKSON: This is just terrific. I think it's pretty much on its own. I think we can, in the interest of time -- I don't want to violate a committee member that wants to ask a question, but I think you're right on target here.

MS. KLOOS: Thank you.

DR. TUCKSON: Really, your time here was worth it for you, I hope.

MS. KLOOS: Right. I think it was for me as well. Thank you.

DR. TUCKSON: So you'll follow up. Thank you very much.

Ann Cashion, C-a-s-h-i-o-n, President, International Society of Nurses in Genetics, ISONG. And we have always appreciated ISONG's involvement with this committee and we've always learned and benefitted from everyone who has come before us. Thank you.

DR. CASHION: Thank you. Good morning, Dr. Tuckson and members of the committee. I am Ann Cashion, a nurse scientist and educator and the current President of ISONG, International Society of Nurses in Genetics. Our membership spans six continents and includes nurse clinicians, nurse educators, and nurse researchers. ISONG is a specialty nursing organization dedicated to caring for people's genetic health through excellence in the provision of genetic health services by fostering the professional and personal growth of nurses in human genetics.

There are over 2.7 million nurses in the United States. Of those, approximately 2.2 million currently are practicing as registered nurses. Approximately 7.3 percent of nurses, or slightly fewer than 200,000, are advanced practice nurses. Half of these, or about 100,000, are nurse practitioners who are delivering primary health care services. Compared to other primary health care providers, nurse practitioners are more likely to be practicing in sites serving patients who are economically or socially disadvantaged or in medically underserved areas. The average salary for a nurse practitioner in the U.S. is slightly over $60,000.

This nursing workforce holds great potential for caring for people's genetic health. ISONG has, in conjunction with the American Nurses Association, developed and promulgated the scope and standards of genetics clinical nursing practice. This document delineates the genetics competencies expected for nurses practicing at the basic level, as well as enhanced competencies for the advanced practice nurse. In addition, ISONG is one of over 40 endorsing organizations of the Essential Nursing Competencies and Curricula Guidelines for Genetics and Genomics. ISONG members, along with nurse leaders from the American Nurses Association, the American Association of Colleges of Nursing, the National League for Nursing, and others, are actively working to implement these competencies. Articles have been published in journals, including the Journal for Nursing Scholarship and MCN: The American Journal of Maternal Child Nursing. Presentations have occurred at meetings such as the American Academy of Nursing and the American Association of Colleges of Nursing and will be also at upcoming presentations for ISONG and the National League for Nursing's Education Summit.

ISONG is committed to working towards ensuring that the nursing workforce is well prepared to serve their patients' and the public's need for genetic information. ISONG is committed to ensuring that all individuals have appropriate access to genetic and genomic health care and has approved a position statement defining the role of nurses in ensuring access.

ISONG is eager to work with the Secretary's Advisory Committee on Genetics, Health, and Society as you work to ensure access to the appropriate level of genetics care for all citizens of the United States. This includes its work to examine the impact of gene patents and licensing practice on patient access to genetic technologies. We are committed to working towards the goal that our over 2 million nurse colleagues have the knowledge and skills they need to practice effectively.

Thank you, and if you have any questions, I'm available both today and tomorrow.

DR. TUCKSON: Well, thank you very much, and I appreciate your specificity at the end around supporting and helping us on the patents and licensing. I don't know whether you were here at the beginning of the meeting when we reviewed our strategic objectives and priorities. I for one would appreciate it if ISONG would send us a thoughtful analysis on the issue of the status of professional education in genetics and whether or not you feel like from your observations enough is being done in the private sector to handle all this, whether we have a problem or not from a point of view, or whether or not there are some real gaps here. I think you're in a unique position to help us to think through that. And we keep this on our agenda as an important priority.

Any quick questions from the members?

First of all, your statement is eloquent and stands on its own. Clearly, as I said, we have enormous respect for and know that we can turn to ISONG as a resource on many things.

DR. CASHION: Thank you.

DR. TUCKSON: So thank you on that.

If staff would keep me on track on this, but I would really appreciate it if you would send us, to the extent that you feel comfortable or willing to do it, your analysis on the status of -- things that we need to think about going forward on continuing professional development of professionals.

DR. CASHION: Thank you.

DR. TUCKSON: Thank you. Great.

Next is Gail Javitt from the JHU Genetics and Public Policy Center. Gail?

DR. HUDSON: I'm Kathy Hudson. I'm filling in for Gail.

DR. TUCKSON: See, the trick is that while I ask the people their name, it is to help to move them going to the chair. I wasn't supposed to slow her down.

Kathy, thank you very much for joining us and taking the time to present.

DR. HUDSON: Thank you for having me.

My name is Kathy Hudson. I'm the Director of the Genetics and Public Policy Center at Johns Hopkins University, and almost exactly a year ago, my colleague, Gail Javitt, appeared before you and expressed our strong concern about the inadequacies in genetic testing oversight.

Sadly, little has changed over the course of the last year, and I'd like to take a couple minutes to review what CMS has and has not done and also to respond to some of the statements that CMS has made over the course of the last year.

So briefly, to review, CMS last June told you that a proposal for genetic testing specialty creation was on its way, possibly by early 2007. Fewer than three months later, the agency said no specialty area would be developed.

CMS has given many different explanations for this policy reversal. They told you last November that there was "no evidence" that there was a problem. With respect, we differ.

On the issue of evidence, we fielded a survey of laboratory directors and asked them about their participation in existing formal PT programs. We found that fully a third of laboratories are not participating in existing formal PT programs.

When Congress passed CLIA in 1988, it was gravely concerned about the failure of laboratories to perform PT and its consequences for patient health. For this reason, Congress directed the Secretary to require that laboratories participate in PT unless the Secretary determined that an appropriate PT program cannot be implemented.

Bluntly stated, CMS is following neither the spirit nor the letter of the law. Because of the way in which CMS has implemented CLIA, in order to require PT, CMS first needs to create a specialty, and as you heard, they have now decided not to do that. No specialty. No PT.

CMS has said that the lack of a mandate for PT has no practical effect because there are so few formal PT programs available, and while it is certainly true that the number of tests far exceeds the number of formal PT programs available, to the extent that CMS could require that laboratories participate in available formal programs, it would certainly cause a shift in the situation. And moreover, I think we could predict that more formal programs would be developed. Simple market economics.

With respect to our survey, CMS has characterized our survey findings as identifying pre- and post-analytic errors in genetic testing. And unfortunately, that's an inaccurate representation. Thirty percent of the most common errors identified by labs were analytic errors. Moreover, a strong predictor of whether a lab's most common error is an analytic error is the level of PT performed by the lab. The take-home message is fairly clear: PT matters and many labs are not doing it.

Finally, on the issue of transparency that was addressed briefly in Greg's remarks earlier, in enacting CLIA, Congress directed that the Secretary make the results of PT testing available to the public. CMS has not done this, making it impossible for any external body, yourselves included, to assess the quality of laboratories. There must be more transparency on the issue of laboratory quality.

And finally, CMS has asserted that only a few organizations want the agency to issue a genetic testing specialty when, in fact, over 100 organizations and individuals representing industry, laboratories, patients, and health care providers have called on CMS to move forward. In September, we, along with the Genetic Alliance and Public Citizen, filed a petition for rulemaking with CMS requesting that a specialty be created. Six months later, we have received no response.

In your session today on oversight, I hope you'll focus on the following issues:

First, the need for CMS to move quickly. There's no need to do an inventory. It's pretty self-evident, the importance of PT, and we should move expeditiously forward.

Secondly, we need transparency so that the public can have confidence that the laboratories are performing adequately on PT and have the expertise to ensure accurate testing.

And then the broader questions of a coherent regulatory framework to ensure that all tests are clinically valid before they're offered to patients.

I thank you for your attention.

DR. TUCKSON: Well, we thank you for especially that specificity.

Will you be around this afternoon?

DR. HUDSON: Yes.

DR. TUCKSON: So you will. All right. I think you've raised some extremely important points. I don't know whether, Jim, you are prepared or want to make any clarifying comments before lunch or just let it stand on its own and we'll just grapple with these issues this afternoon.

DR. ROLLINS: This afternoon.

DR. TUCKSON: I mean, that's appropriate.

DR. ROLLINS: Also, I think that probably the persons who are responsible for CLIA would probably be in a better position to address these questions.

Also, number two, I know that in the past that you, as well as, I think, Ms. Berry, met with Mark before he left, and probably it would be a good idea to discuss these specific issues with Leslie Norwalk or her designee who could specifically address these.

DR. TUCKSON: Well, I'll tell you what we'll do then -- thank you for that. I think what I'm interested in -- other members of the committee will have their own interests -- is not so much -- although, I mean, clearly there was some animation around whether CMS has responded or not, and I think that's its own set of issues. I'm much more interested in the generic issues of the role of proficiency testing in this chain of events and whether or not those issues are being attended to appropriately. I'm much more interested in the substantive issues than in the political issues.

So I think that this is actually very important and we should come back to these questions in our afternoon discussion. We may want to draw on you for some input. So thank you for that.

I think Judy Yost will be around this afternoon as well. So we may hear some more there.

As I said, it's always painful to hear that an agency may or may not be responding, and I don't know any of the facts on that. But I'm much more interested in the substance, which I think we've gotten some important granularity in terms of the steps in the process that is worthy of our attentiveness, regardless of any other issues.

Oh, good, Sharon Terry again.

MS. TERRY: With a different hat.

DR. TUCKSON: With a different hat. It's always good to have more than one hat.

MS. TERRY: Now that we can do something besides just nondiscrimination, thank you for the opportunity to present brief comments on behalf of the Coalition for 21st Century Medicine. Though I often appear before you as either a representative of the Genetic Alliance or the Coalition for Genetic Fairness, I believe that representing this new and diverse coalition is important since it represents our commitment to collaborative solutions.

Founded in late 2006, the Coalition for 21st Century Medicine represents 22 of the world's most innovative diagnostic technology companies, clinical laboratories, researchers, physicians, venture capitalists, and over 30 patient advocacy groups, including the Genetic Alliance's coalition of 600 advocacy organizations, all linked together by a common mission to develop advanced diagnostics that improve the quality of health care for patients.

The coalition believes that innovation and quality care are the keys to 21st century medicine and that timely access to new information by physicians and patients is critical to improving the quality of care and providing personalized medicine. The coalition shares HHS's focus on personalized medicine and the Congress' and FDA's goals of assuring that treating physicians and their patients have access to safe, accurate, and reliable information to assist in decisionmaking. In light of that, we support the Congress and the various agencies striking an important balance between regulation and innovation.

The coalition is pleased to be in an ongoing and constructive dialogue with FDA. We are grateful to FDA for its willingness to exchange ideas about their initiatives around IVDMIAs and ASRs. We met with FDA leadership in December, presented at the February 8th public hearing, and submitted dozens of formal comments on specific draft guidances.

In summary, the coalition is concerned that if implemented in their current form, the draft guidances for both IVDMIAs and ASRs may result in adverse, unintended consequences. We are concerned by the ambiguities that exist under the current draft guidance and feel that labs will need more clarity moving forward. We urge FDA and the Department to continue its dialogue with patients, providers, and innovators and believe that this dialogue can influence and inform Congress' heightened interest in enacting new law in this sector. It is clear that there is a real chance that congressional action and the resulting novel or substantially modified statutory authority may ultimately supersede the draft guidance in important ways.

In the interim, the coalition will continue to educate key stakeholders about the importance of innovative new diagnostics and the role in reducing health care costs, providing new pathways to relieving the burden of disease, and personalizing medicine. Our overall goal is to help determine the most appropriate pathway for regulation of IVDMIAs and ASRs, while preserving a forward-looking innovation environment in which patient safety and access are the highest priorities.

Various legislative initiatives are being introduced and may be enacted this year that establish different regulatory provisions. Earlier this month, Chairman Kennedy and Senator Smith introduced the Laboratory Test Improvement Act. The coalition has worked with HELP Committee staff and leadership and we share Chairman Kennedy's interest in safeguarding all laboratory tests.

However, the coalition remains concerned about particular elements of the bill. As mentioned above, the coalition feels strongly that any new regulatory environment must consider how incentives to encourage innovation are affected by this bill and how that impedes access.

We believe that the Laboratory Test Improvement Act may hinder such innovation by regulating all laboratory-developed tests as class II medical devices subject to potential premarket review. While the coalition supports the registry concept outlined in the legislation, we are concerned by the provision deeming all laboratory-developed tests to be medical devices. We worry a great deal about the smaller labs and the incredible service they provide to underserved communities of patients, particularly those with rare diseases. The coalition is committed to ensuring the safety of all tests, but regulating all laboratory tests as medical devices and laboratories as device manufacturers would present enormous difficulties for labs and the FDA.

The coalition has also been pleased to work with Senator Obama and his staff on the Genomics Personalized Medicine Act. We encourage the development and use of high quality LTDs, including genetic tests, and support the flexible approach to regulation introduced in Senator Obama's bill.

As the legislation process moves forward, the coalition will continue to emphasize the importance of the Clinical Laboratory Improvement Amendments of 1988 in ensuring that patients and physicians have timely access to these diagnostics. I won't go into the issues around that act since Kathy just outlined them, but we agree very much with the details that she gave you.

In conclusion, the Coalition for 21st Century Medicine is committed to working with CMS, FDA, and the Congress to ensure that regulation of laboratory-developed tests is provided in such a way that regulation supports innovation and access to diagnostic test services for patients, as well as reliability and quality.

As a result, we have formally requested via letter to Dr. Tuckson that Secretary Leavitt convene a meeting to engage the key stakeholders, members of Congress, and agency officials to make sure

that the wide range of views are heard and considered and that appropriate coordination is achieved among these initiatives before any final decisions relating to a new regulatory provision are put into place.

We look forward to working with the Secretary's Advisory Committee on Genetics, Health, and Society and all parties involved in these vital matters of public health, patient safety, and personalized medicine. Thank you for the opportunity to share our thoughts.

DR. TUCKSON: Sharon, thanks a lot. We're going to have to roll to lunch. First of all, I appreciate that. But I think the real question to get from you is when you sort of see us lay out that outline around oversight and where pieces plug in, if you could give Andrea sort of where you see it fitting in and being pretty specific there, I think you'll get involved in our deliberation in a much more effective and quick way.

MS. TERRY: Sure.

DR. TUCKSON: Ultimately, at the end of the day, we will be at the end of it sort of figuring out what do you do with it all. But I think you really need to influence us well upstream. So if you'll get with Andrea, I think it will be important to sort of fit it into the outline.

MS. TERRY: Sure.

DR. TUCKSON: Thank you so much. We really appreciate it.

By the way, Debra, can we get to you later today or tomorrow? Because I know you want to testify. We've got to get the committee to lunch and their stomachs are getting louder.

But I do want to hear from David Mongillo from the American Clinical Laboratory Association because David did sign up for this particular session early on. David, we appreciate it. We have also appreciated the fact that ACLA has provided comments to us in the past and have always been well received. So thank you.

MR. MONGILLO: Thank you, Dr. Tuckson. We appreciate coming here.

I am David Mongillo, Vice President for Policy and Medical Affairs at the American Clinical Laboratory Association. Many, if not all, of our members perform genetic testing and thus have a keen interest in the issues addressed by the committee.

You're going to hear some redundancies from the 21st Century Coalition comments, but I think it's important to hear the vital nature of these comments.

We wish to focus our comments on recent activities related to the regulatory and legislative oversight of laboratory-developed tests. FDA recently proposed new guidance on in vitro diagnostic multivariate index assays. IVDMIAs play an important role not only in current genetic testing, but will continue to play an important role in future genetic testing.

FDA held a meeting February 8th to hear public comment on the draft guidance document. Over 300 representatives were present at the public meeting, and over 30 comments were received from clinical laboratories, manufacturers, government officials, academia, and others.

Some common themes emerged from the presentations, namely, that all laboratory tests should be safe, clinically valid, and effective, a theme which ACLA certainly agrees with and endorses. But also communicated to FDA at the public meeting was that the FDA guidance, as proposed, raised concerns and questions that needed further clarification and stakeholder involvement.

Two important bills were introduced in the Senate this month. Just this past Friday, Senator Barack Obama's bill, the Genomics and Personalized Medicine Act, was introduced, and Senator Edward Kennedy's bill, the Laboratory Test Improvement Act, was introduced on March 14th. Both bills address issues associated with molecular and genetic test oversight.

ACLA was one of 25 organizations who sent a letter on March 16th to Senator Kennedy respectfully requesting additional time for more careful analysis and discussion of the bill, and I think you have a copy of that bill with your comments. The sign-on organizations represent professionals and entities comprising virtually the entire spectrum of laboratory and medical interests, including genetic disorder patient groups, genetic and molecular practitioners, genetic-oriented policy groups, pathologists, laboratory technologists, and clinical laboratories. It's interesting to note that the organizations that signed the letter may have varying views on the need for additional oversight of laboratory-developed tests; however, they are fully united in the request for more time to provide feedback and discuss pathways that will not have unintended consequences on patient care and laboratory services. The groups are further united in the opinion that any new legislative initiative in this area should be carefully crafted to focus on the specific areas of concern and not be so broad as to encompass laboratory tests that are clinically established or that are serving a valuable purpose for rare disease groups and public health needs.

Our overall message today is simple. Let's not rush to solutions without thoughtful deliberations on all the issues associated with the need for increased genetic testing oversight. This committee has the professional expertise and the understanding to contribute significantly in advising these issues as they are deliberated. I think the HHS charge this morning and the discussions that will follow this afternoon are certainly a major step in that direction. ACLA asks that the SACGHS communicate your desire to provide input on these issues before they are finalized.

We thank you for the opportunity to comment and look forward to working with the committee and the agencies on these important issues.

DR. TUCKSON: Terrific. Well, thank you so much. Again, I would continue to urge your organization, as we did just a moment ago. Try to track with us what happens this afternoon and then find places that you think you might want to comment as we get in because that's really the way to do it.

MR. MONGILLO: We'll do it.

DR. TUCKSON: Terrific.

So we've got to go to lunch. So, members, your lunch is outside. For those who are not on the committee, I am informed that the hotel serves lunch at the renowned Mount Clare Cafe, which is around the corner from the ballroom, and the Garden Restaurant, which is also well known.

Now, here's the deal. It's 12:33. We're supposed to start at 1:15, but that's not fair to you. So we're going to start at 1:20.

(Laughter.)

DR. TUCKSON: Which means that you'll actually start at 1:25. But the problem is that we've got people calling in at exactly 1:30 and we've got some table-setting to do before they call in, and they don't know that we're late and we can't reach them because they're on the beach.

(Laughter.)

DR. TUCKSON: So you have to go right now. So bye. I'll see you at 1:20.

(Whereupon, at 12:33 p.m., the meeting was recessed for lunch, to reconvene at 1:20 p.m.)