Summary Report from the Conference on Promoting Quality Laboratory Testing for Rare Diseases: Follow-up and Future Activities
D. Joseph Boone, Ph.D. and Stephen C. Groft, Pharm.D.

DR. TUCKSON: We're going to move forward and invite Dr. Joseph Boone, Assistant Director for Science, Division of Laboratory Services, CDC, and Steve Groft, Director of NIH Office of Rare Diseases, as they help us to look at the issue of the summary report from the Conference on Promoting Quality Laboratory Testing for Rare Diseases. You will remember that they had this conference in Atlanta in May of '04. They are making plans for a second conference. The executive summary of the proceedings is in Tab 5 of the briefing book.

While the conference was conceived as a plan to address access in quality of laboratory testing issues for rare genetic diseases or conditions, it wound up identifying a number of issues beyond the quality assurance. The group soon expanded the conference to include other topics of interest, many of which intersect with the interest of this committee. Therefore, we will be learning about that and seeing how it dovetails with our activity.

Thanks a lot, Joe.

DR. BOONE: Thanks very much.

It is unfortunate that Dr. McCabe is not here, because some of the things that we're going to be presenting are certainly relevant to this precursor of this committee. We are really addressing some of the issues that have been raised before. Particularly the issue of translation of research findings in clinical practice, and the issue of access in quality of laboratory services.

As Dr. Tuckson mentioned, we did have a conference in May of 2004. That conference did address primarily a set of issues that was raised by this committee previously. It has partners, Emory University, NIH, and CDC. That's the reason that we're doing this tag team presentation today.

Our definition of quality was really in terms of CLIA. We felt like at least the minimum requirements should be a certified laboratory. So the two areas where we were most concerned were research-only laboratories, and those laboratories that are located outside of the U.S., and the quality of the services that they might be providing to U.S. citizens.

So the basic things that we were looking at was to ensure the quality of access testing, and we were concerned about the research laboratories that might be providing patient testing without a CLIA certificate. We were also concerned about the translation of gene findings in clinical practice. We had a number of other issues that were concerned about.

You have these charts in your books, but the main thing is that in terms of the U.S., 78 percent of the tests are being done in the U.S., 22 percent are being sent outside of the country, and 33 percent of the testing on gene tests are for research-only laboratories. That's the test themselves.

If you look at the distribution of laboratories, research-only laboratories account for about 40 percent of the U.S. laboratories in GeneTests. Non-U.S. laboratories count for 30 percent of all the labs listed in the directory. That was in 2004. The data haven't changed very much since that time.

Another thing that's important to look at real quickly is the fact that of the things that are tested for, many of those tests are available from only one laboratory, or from a very small number of laboratories, which makes some of the quality assurance practices that we'd like to have in place difficult to do.

There are very few tests that are actually available through the College of American Pathology survey program. Similar in Europe, there are very few tests that are actually being monitored in a quality assurance mode.

So in the summary slide, I think the main thing to focus on here is the fact that we're falling further and further behind in terms of development of GeneTests. Rare disease associations are being found at the rate of about 20 per month. The new testing that we are able to incorporate is about ten per month. So we're running 50 percent behind in terms of developing new tests to address the conditions that are being found in the gene findings. That gap really does need to be closed.

So the results of our first conference was that we actually formed a North American Laboratory Network for Rare Disease Genetic Testing. That network is comprised of laboratories that are all CLIA certified, and will report the limitations of the tests in their reports. They are going to work collectively to increase the development of new tests to foster research and clinical laboratory partnerships and serve as a back-up resource for additional tests.

There was an organizational meeting, which Steve is going to talk to you about in a moment. But there were about six laboratories that formed this original alliance of testing laboratories.

In addition, the American Society of Human Genetics and the Office of Research Protections agreed to provide education to researchers and IRBs, which is something that was really needed. NIH has a pilot program to fund translation of research tests into clinical, applicable tests. That program, we want to see that expanded in a logical manner. Then we plan to have a meeting later this year, which Steve will tell you a little bit about.

So we're on a pathway I think that is the right pathway. We're not confused. We know where we're going. Steve is going to tell you a little bit about how we might get there.

DR. GROFT: Thank you very much, Joe.

You saw the stop lights, red lights, green lights, yellow lights. Sometimes I think we're working all at one time, so we're not sure how we're going to get there. As you will see in the last slide in the presentation, that's even more of the confusion that we're adding into the situation. I'll try to get this moving.

We do have a meeting planned on March 17th prior to the American College of Medical Genetics to really start to crystallize and finalize many of the discussions that have been held previously, both at the meeting last year in May at the Centers for Disease Control in Emory University in Atlanta. A number of discussions have been held by a lot of participants since then to look at presenting this at the September, 2005 conference here in Washington.

We have been working on identifying major issues in target audiences that need to be at the meeting in September. We'll be looking at the conference agenda, and then assure that there is broad based participation in the meeting in September. We still are in the planning stages, but things are coming together rather nicely.

It seems like for the first time we've been able to get many of the major participants who we had to get together to really affect an effort that would have some outcomes that could move forward. We are getting together here finally, so it's good to see.

At the conference in September, again, it will be in Washington. It will be a two-day session. We'll have plenary sessions and reviews. And again, we're working all of these issues up that Joe had talked about as far as the vision and other things that we need to discuss to give us direction, movement, and the momentum to move forward.

A couple of the issues that we need to work on are trying to establish the priorities for developing genetic tests for rare diseases. There are so many disorders that we could look at and really start to work on. We really have to try to identify those priorities and the criteria for selecting them. It is just an area that we hope to hear from a lot of people on how we're going to go about this.

The conditions for the clinical laboratory participation. We currently at the Office of Rare Diseases have a small program with the National Human Genome Research Institute within the Clinical Center to develop these genetic tests for about four rare disorders last year that we did under the direction of Bill Gault, the Clinical Director for the Human Genome Research Institute.

This year, we hope to expand that to about 16 to maybe 20 more tests that we will develop, mostly for the use of the Intramural Research Program. So we wanted to go forth and start in the intramural program, get some direction, some experiences, and then move possibly into the extramural program.

As we were moving forward last year in developing these genetic tests, we came to the conclusion that this was something that is quite capable of being done in the extramural program. Now we are looking for partnerships within the NIH system to expand the whole program to increase the number of genetic tests that are developed for rare disorders.

When you have a total of 6,000 or 7,000 rare diseases, it is quite a task. Where do you start? How do you continue? How do you gain the interest? But there certainly has been a lot of interest in seeing this move forward to have the tests move out of the research stage into the stage of clinical accessibility for the public.

The next three slides that you have and that are available for anyone who may be looking in through the website, is we've talked about the long-term visions and the short-term visions for what we want to accomplish, and where we want to go, so I won't spend too much time on that. I know the day is drawing to a close, and people have their planes.

There are a number of areas that we want to talk about, and we will discuss the successes. How are we going to measure it? How are we going to identify the successes for the patient's families and the providers, as well as the laboratories and the testing groups. Then finally the success of the system and the services that will provide these services to the public.

We hope to evaluate whatever success we're able to achieve through pre and post-surveys of the laboratories, the consumers and advocacy groups, the Centers for Medicare and Medicaid Services, and other payers, and then to monitor the tests that will become available, and to monitor the quality of these tests, as well as any adverse events that may occur. That seems to be a major concern these days, as they should be.

Then we hope to lift the roadblocks and to remove them to create the models that will generate the energy to move forward towards the solutions. Again, we know there is a lot of passion involving individual rare diseases, but I think we have to look at this in the sense that we are not going to be able to do all rare diseases at one time. We will start in a systematic fashion and continue to move through and to complete as many as are possible at the present time currently that are in the research stage or in the research laboratories.

I guess we have been hearing about the need to do this for many years from a lot of the patient advocacy groups who of course would like to have a genetic test available for their disorder.

There is always the concern that if they are available from a research laboratory, that the research money will dry up, and the project will just die. It may never be available for use in the clinical services. So I think those are some of the areas that we're looking at, and some of the needs that we're trying to work with as we move forward.

This is a slide that we have tried to put together. We could have put all those different lights in there too as well. You see the number of partners that we are dealing with. Actually it has been very nice progress I think as we move forward from the planning last year for the May meeting in Atlanta to where we are today.

The number of groups that are involved are numerous, yet there has been a good sense of a need to move forward quickly and as expeditiously as possible. So I think we'll just end it with that one and try to answer any of your questions that you might have.

DR. TUCKSON: Thank you both. Very, very important work.

The floor is open. Any questions?

DR. WILLARD: Just a point of information. Are there precedents or other examples where HHS steps in to prioritize development of tests for diseases that affect, by definition in this case, a very, very small number of its citizens?

DR. GROFT: I don't know of any directly, although looking back on when we started with the Orphan Drug Act back in 1983, we tried to identify compounds that were available on the shelves of companies that weren't being developed.

We tried to provide incentives. That's what happened through the Orphan Drug Act, incentives. But we also tried to identify compounds that would be useful. We went about then funding research, trying to support research for those areas.

So I think the scientists, the laboratory people will identify those. As I mentioned, some of the first areas we'd like to work with are those that are already in the research laboratories, and maybe could move over to the clinical side.

DR. BOONE: And we've talked about the federal process, but we also have a private sector process that's engaged in this overall activity with us. There were some 50 people that were at our original meeting, and we hope to have maybe as many as a couple hundred people at the September meeting.

We get the same message from the people in the private sector, that the rare disease community is coming to them with funds in hand wanting tests developed. They simply don't have enough capacity to move these tests through the system.

DR. GROFT: And for the most part, we probably will not establish the priorities completely. I think this is where a community will come forward. We are looking for a cooperative effort among the patient advocacy groups, the laboratories, the NIH, the CDC, and all of the government agencies who have to work together on this issue.

So there will be a lot of people coming together. In the last slide, you could point there as to who is going to bring the tests, the need for certain tests, and everyone will be bringing the tests forward to us for consideration. But we will not be the sole source of funding.

MS. ZELLMER: I just had a quick question. Just based on what you said then, are primarily then the barriers to getting these tests developed the laboratories just not having the capabilities? Or are they more financial? Or both?

DR. BOONE: It's a little of both. I mean, Dr. Ledbetter at Emory University indicates of course there is enough capacity to do these tests within the United States, but some tests are going abroad. You have to ask the question, why is that occurring. I think there are several reasons that that is occurring.

I really applaud NIH for taking this initiative to try to put the researcher with the clinical lab in a partnership so that that transition period hopefully will take less time, and we'll be able to move tests more rapidly through.

This really is a network that is starting to build, too, because there are a few labs that are in this. If the pilot really works well, then certainly we can engage I think more genetic testing laboratories in this process.

DR. GROFT: I think with so many rare disorders, there are so many possible conditions and situations that exist that you can't say it's this or that. There are many, many different possibilities here.

But we are hoping to have some pilot projects involving different laboratories so we gain the experiences of commercial laboratories, as well as CLIA-certified laboratories, some that are in so-called ultra-orphan disorders with a very, very small prevalence of diseases that we'll look at to see how things are done and how we might be able to just use those experiences to extend out to the entire community.

DR. TUCKSON: Thank you both. We very much appreciate it. We look forward to updates after the meeting. Thank you both.