Initiatives of the National Institute of Standards and Technology (NIST) in Clinical Diagnostics Standards Development
Willie May, Ph.D.

DR. TEUTSCH: Thank you very much, Dr. May, for being here. We look forward to what you have to tell us. Thanks so much.

DR. MAY: We don't have much time, so let's just get at it. What I would like to talk to you about this afternoon is our organization, our basic mission, and some of the new initiatives that we have. Specifically, I will talk about why NIST would be involved in bioscience and health since we are not NIH, we are not CDC, and we are not FDA. I will talk about some of our current activities in the area of bioscience and health.

I will just say now that standards for genetic testing are a very, very small part of the portfolio but one that perhaps you can convince us to increase.

Finally, I will talk about how we are connected to the international measurement standards community.

Our organization was born, if you will, a little bit more than 100 years ago and charged with providing the measurement standards infrastructure to support manufacturing, commerce, and the makers of scientific apparatus, to work with other government agencies, and to support the academic sector. It is amazing; if you were to look now at the things we do, it is almost like this chart was given to us last year. This still remains the focus of a lot of our activities.

Now, some of the early drivers for some of our activities. We were in the midst of the Industrial Revolution, and people noticed that construction materials were not of uniform quality. Also, there were eight different values for a gallon if you drove from the East Coast to Chicago. Standards were needed for the electrical industry. Scales were not standardized and they were often biased in favor of the seller, as you might imagine.

There were needs from chemical composition, dimensional, and metrology standards to support the railway system. In other words, lots of trains were jumping lots of tracks.

The thing that was most alarming, we being who we are, is we didn't like having to send our instruments abroad to be calibrated. So those things led to the inception of the National Bureau of Standards in 1901.

Since we are not the lead agency for health, the environment, or food safety and nutrition, and we have this arcane mission of being responsible for the nation's measurement standards, to remain a viable and productive organization we have had to change the focus of our activities continually to focus on major problems of society.

Today our organization has four major components. The NIST laboratories are the remnant of the National Bureau of Standards. We manage the Malcolm Baldridge Quality Award. We have something called the Hollins Manufacturing Extension Partnership and the Technology Innovation Program, which used to be the Advanced Technology Program. Perhaps after the session, if anyone has any questions on any of these extramural programs, I can share those with you.

Our mission is to promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve quality of life.

If you really were to look closely, this part and that part change. The words change in almost every administration. But these three bullets have not changed to any substantive effect over the last 100 years.

The NIST laboratories are responsible for maintaining the expertise and facilities for providing this measurement standards infrastructure to support the U.S. That work is carried out by what we call the laboratories, the Chemical Science and Technology Laboratory being one of 10 of these.

As you can see, we are organized pretty much like a university campus. We do what some people might call academic-type research, but that is to support the dissemination of the measurement services products that we disseminate.

Primarily, lots of work goes into the realization of the seven basic units of measurement, things like improving our realization of time. Right now the NIST Atomic Clock is accurate to one second in 30 million years. We are working on clocks now that we think will improve this by three orders of magnitude.

You might think, why would you do this? My watch works fine. Well, things like GPS and a lot of things you don't think about, like interstellar travel and so forth, are very dependent very precise realization of time and frequency measurements.

The last physical artifact that exists is the kilogram that sits in the basement of the BIPM in Paris. If you have been looking at a lot of the editorials in the popular press lately, you will find that the kilogram is said to be losing weight at about one part in 10^8 per year. We don't really know that that is happening. All we know is that the mass of the kilogram relative to the mass of about 30 other prototypes based on that seems to be changing over time. So the relationship between them is changing, and that is a practical reason for changing.

There are also just pure scientific reasons that are leading the community to try to establish what we call the electronic kilogram. There is an approach to something called the Watt Balance. The new redefinition will be based on Plank's constant, most likely. But to lock that time, we will take this kilogram and then have a device called the Watt Balance. Different countries have different realizations of this to balance electrical force and mechanical force to try to transfer this.

Again, that realization has to agree to about one part in 10^8. Right now, we are about one to two orders or magnitude off from that. So that has to be completed by 2011 if the kilogram is to be redefined.

But we also serve a much broader community with constantly changing measurement standards needs.

NIST has traditionally focused its research and measurement service activities on the physical science and engineering disciplines. But bioscience and health has now been identified as an area for significant emphasis and growth at NIST.

Why NIST and the biosciences. First of all, as the NIST leadership has looked at our mission, we feel that it is congruent with our mission and indeed our mandate to support U.S. industry and other stakeholders with overcoming measurement standards-related challenges in the biosciences, to provide confidence in results from measurements of complex biosystems, and to enable and facilitate realization of the maximum economic and broad societal benefits of innovation.

Now, Mike Amos and I have this discussion all the time where he says, NIST has to be involved for innovation, and I say, no, we don't, Mike. Not at all. Innovation is going to take place whether NIST exists or not. However, we maintain that by having this infrastructure to support comparable measurements over space and time we will provide the infrastructure to allow society to gain maximum benefit out of these new innovations.

The other reason that we are doing it is, an emphasis of the administration is a better understanding of complex biological systems. I think this will continue into the next administration. The executive branch, let's say.

Other agencies come to us. This is just one quote. It's from Anna Barker, the deputy director of NCI.

There is an oversight committee that NIST has called the Committee on Advanced Technology. We have heard from two of its members that NIST should also expand its activities to support the biosciences.

Actually, we have been involved in bioscience-related activities for quite some time. Back in the 1920s a collaboration began between NIST and the American Dental Association that led to a lot of the innovations in dentistry that we take for granted now. Things like polymer composite dental fillings and the air turbine drill, found in almost all dental offices, were developed by a number of employees of the American Dental Association who work at NIST full-time. There are about 30 people. Many people don't know they aren't NIST employees because they work there full-time.

In the 1920s we also started a program in radiation physics which focused initially on X-ray calibration and now includes standards for mammography and radionucleides for radiopharmaceuticals.

We started our program in oncodiagnostics in the 1970s with some support from NIH to provide primary references for electrolytes and metabolites. So, cholesterol, uric acid, glucose, electrolytes, calcium, sodium, and so forth. Then, later, in the 1980s, we began having serum-based standards for those. Around the turn of the century we began to focus on biomarkers for proteins, peptides, and DNA.

This is an example of some of those small molecules, primarily electrolytes and metabolites, that we have had standards for for a number of years. By standards I mean reference measurement procedures and, obviously, certified reference materials or standard reference materials.

Then, about 10 to 15 years ago, we began to focus on more challenging biomarkers. These are some of the things that we have worked on. As you see, two of these might be considered genetic standards, but my colleagues will talk to you about some of the more in-depth details of expansion in this area.

NIST spends a little more than 10 percent of its appropriated funds on bioscience-related activities by our own self-declaration. Now, of this, around $38 million is focused on biosciences. Only about $10 million was appropriated for that. The other money has come as the result of decisions by individual laboratory directors to reprogram funds into this.

Right now, we are in the process of developing a strategic plan not only to support growth of our program in the biosciences but also to do a better job of directing some of the funds that we already have. Right now, to be quite honest, each laboratory has its own program. To get maximum impact out of the resources we have, we are going to try to coordinate this in a much better manner.

I will just go through some of the activities and projects that we have that support health care.

So, what is the typical role of an organization like NIST. We see that all the national metrology institutes around the world have scientifically sound, metrologically-based -- not weather -- measurement science-based competencies and measurement capabilities that are vetted internationally. That underpins the delivery of a number of measurement services, one of which is certified reference materials. Standard reference materials is the NIST brand name for the certified reference materials that we produce.

Now, the Treaty of the Meter was established in 1875. It developed this collegial group of national standards institutes around the world, those that existed. Of course, that was before NIST existed. NIST or NBS, joined that in the early 1900s.

In 1999, though, there was a mutual recognition arrangement that was established that required three things. All national standards institutes like NIST were required to declare and document the measurement capabilities that we use to deliver the services that they provided.

By signing this, you also said that you would agree to participate in very formal international comparisons so that you had some evidence to support the claims you were making and, further, you would maintain a quality system to underpin your dissemination of the services that you deliver using these techniques that you have claimed have been internationally vetted and compared. This mutual recognition arrangement now has been signed by over 200 national measurement institutes or designated institutes around the world.

This is an example of a comparison for creatinine and serum. This is the European Union laboratory, Korea, the U.K., NIST of course, and the German laboratories. This basically shows how well our capabilities for providing reference measurements for creatinine serum agree with each other.

This is a more recent one that was completed this year. This is cortisol in serum and progesterone in serum. Japan, the U.K., China, the U.S., Germany, Korea. Then, progesterone, the same laboratories, except Australia is involved, and Mexico.

In this example certainly, if there was a CRM that was developed by Mexico based on this analysis, there might be reason to question it, if you will.

The MRA is about documenting measurement capabilities that national metrology institutes maintain and looking at how well those measurement capabilities compare with each other.

Also around 1999, there was this European Union directive that said that the traceability of values of assigned to calibrators or reference materials must be assured through available reference materials of a higher order. The U.S. IVD manufacturers came to NIST and the metrology community and said, we need help with this because without that we won't be able to sell our products in the European Union.

So we convened a meeting at NIST among all the stakeholders. One of the recommendations was the establishment of a global consortium of IVD manufacturers, professional societies, national metrology institutes, and regulatory bodies. This organization became named the Joint Committee on Traceability in Laboratory Medicine. Three principals in this were the International Committee on Weights and Measures, which represents the national metrology institute community; the International Federation for Clinical Chemistry, which represents the professional community; and the International Laboratory Accreditation Corporation, which represents the accreditation community, if you will.

The product from this is a database of higher order reference measurement procedures, certified reference materials, and laboratories that provide reference measurement services to the clinical chemistry community.

I will just show one of their work products. A work product other than this database is the comparison of standards that are in that database to see how they compare with each other. As it turns out, the standards three years ago for cholesterol came from only two places. There were a number from NIST and a Japanese laboratory, and this just shows how they compared with each other. If one were to select randomly any of the certified reference materials in the database, they agree to within less than 1 percent of each other.

This shows also two reference measurement procedures for cholesterol that are identified in the database, and there are only two. This is how well they agree with each other.

So the world is changing, and we realize that we must change at NIST. Mike Amos is going to talk about this, so I won't say a lot about this except to say that one of the future thrusts for us is to look at tools for what we call visualization of disease signatures and our new initiative for 2010 and beyond. It will have two areas of focus. One is quantitative medical imaging and protein measurement science.

At this point we don't have standards for genetic diseases in there, but after discussing it with you, if the general capabilities that we have won't support that, then there is an opportunity to amend our current plans.

So, thank you for your attention.