Legacy of the Secretary's Advisory Committee on Genetic Testing
Edward R.B. McCabe, M.D., Ph.D.
SACGT and SACGHS Chair

DR. McCABE: The next section is where we really begin to talk even in more concrete terms about the development of the SACGHS priority issues and work plan. I will be giving a presentation and will review the recommendations of the SACGT and the activities that were in progress at the time that the charter was not renewed for that Committee. Then Sarah Carr, who as we said yesterday also served as the Executive Secretary for the SACGT and now is fortunately for us our Executive Secretary, will provide a summary of the priority issues identified by SACGHS ex officio agencies and departments as warranting the Committee's attention.

Since there are individuals who were involved with SACGT, both from the Committee and the ex officios, if going through, there's something you'd like to add to my presentation to clarify or in any way add to my discussion, please just let me know and I'll be happy to have you include your comments.

So the SACGT was chartered for four years but it took about a year to really get the group together. We functioned as a Committee from 1999 to 2002. The mandate was to identify policy issues raised by genetic testing and to make policy and procedural recommendations to the Secretary of Health and Human Services on how such issues should be addressed, including the safe and effective incorporation of genetic technologies into health care, the effectiveness of existing and future measures for oversight of genetic tests, and research needs related to the Committee's purview. So I think you'll see that the mandate for this Committee is substantially broader than before.

The policy recommendations of SACGT included reports, a report on oversight of genetic tests and methodology for classifying genetic tests into different scrutiny levels. We also had letters to the Secretary. Our first letter to Secretary Shalala and then with the new Administration, our first communication was Secretary Thompson, both had to do with genetic discrimination and health insurance and employment because as we had been asked by the Assistant Secretary for Health, Surgeon General Satcher, that we reach out to the American public, the American public was extremely concerned about genetic discrimination. We also sent letters to the Secretary about gene patenting and licensing and then secondary subjects and research.

So regarding the report on oversight, the oversight issue addressed was addressed at the request of the Assistant Secretary for Health, Dr. David Satcher. He charged the Committee in our first meeting with having a report to him as soon as possible. I think it may have even been like a three- or six-month deadline. We did not meet that but had it to him within the first year. That was a very specific charge which focused our energies over the first year.

It involved a comprehensive assessment of the adequacy of oversight of genetic tests, a broad multifaceted public consultation process, and a consideration of all options. It resulted in "Enhancing the Oversight of Genetic Tests: Recommendations of the SACGT" -- that was the title of the report -- and we recommended increased federal involvement in the oversight of new genetic tests through a flexible regulation by the FDA, augmentation of Clinical Laboratory Improvement Amendments, and development of a collaborative postmarket data collection effort by the CDC, and I think it's important to note that we did talk about flexible regulation by the FDA. There was concern that by putting this recommendation in place, we could shut down testing and we talked about new tests versus existing tests.

There were several iterations of developing a methodology for this, and as each of these was tested, there were certainly -- the first couple went by the wayside because of concerns that they did not really adequately address the needs and were difficult to implement when they were tried in specific testing examples.

I think many of us, and now I'll speak as an individual and not as the chair of that Committee, but I know that I was evolving to feel that what we really needed to deal with was labeling and that regulation could be very difficult to implement. I know the FDA has moved forward with this and perhaps they can bring us up to date with how that has continued, but we were beginning to talk about labeling as being extremely important and thinking in analogy with a Physician's Desk Reference or a PDR for genetic testing. That had come up in group discussions.

So as I mentioned, FDA is presently considering developing a proposed rule classifying analyte-specific reagents used in high-risk in-house tests, including genetic tests as Class II special controls or Class III premarket approval devices, depending on their intended use and risk profile. CDC and CMS are in the process of preparing a Notice of Proposed Rulemaking to develop a genetic testing specialty under CLIA, and we heard this morning that that is moving forward and the CLIAC will take this up again. I guess actually what we heard was that this had not moved forward as I have here, but that the CLIAC will revisit it at your next meeting.

Is that correct, David?

DR. FEIGAL: That's correct.

DR. McCABE: Regarding the methodology for classifying genetic tests, SACGT considered several options for classifying genetic tests but concluded that classifying genetic tests based on a limited set of elements applied in a simple linear fashion for oversight purposes is infeasible, and part of the problem is that the same test used in different contexts, used when there's a positive family history, used when it's in a counseling process for a single family or used in a population-based screening process, may perform quite differently, has different demands, and may be ready for one context but not for others. So it's not the test, it's the test in addition to the context in which that genetic test is used.

SACGT's decision to defer further work on methodology was also based on significant progress made by FDA to develop an innovative regulatory process for genetic tests, including a template for facilitating and ensuring appropriate review of relevant data.

Letters to the HHS Secretaries included, as I mentioned, genetic discrimination, to place a high priority on the passage of federal legislation prohibiting genetic discrimination in health insurance and employment, and that that was a high priority.

I'll add parenthetically that one of our letters in earlier attempts at passage of these bills on the Hill, one of those letters to the Secretary from SACGT was blown up into a poster and used to try and move that forward. So we're very pleased that that is moving forward, at least in the Senate.

Gene patenting and licensing. We recommended that there be conduct of a study to determine whether certain licensing practices are adversely affecting access to beneficial genetic tests. This was a discussion that was had with parties representing a variety of perspectives on this. It was a quite heated discussion, as I recall, and we have heard some of where that has moved.

Secondary subjects to develop guidance to help define situations in which secondary subjects, meaning family members of primary research subjects, become human research subjects whose consent must be obtained or waived, and certainly we heard more about that from Kim this morning as well.

Reports that were in development. The HHS' effort to advance knowledge of genetic tests, genetic education of health professionals. We've heard again in this day and a portion of the importance of education of health professionals about genetics. Public understanding of genetic testing, informed consent and clinical and public health practice, reimbursement of genetic education and counseling services, development, translation, oversight, availability and accessibility of genetic tests for rare diseases.

Again in my role, along with the other two members of the SACGT who were appointed to this Committee, I think, and sort of under the subheading of lessons learned, that we worked very effectively when we were focused on, as a Committee, the original recommendations during that first year. I think we had some more difficulty finding our way and then, as we went out into work groups and became somewhat diffuse, I think it was much more difficult for us to make progress, and I would encourage this Committee to prioritize the needs and focus on one or at the most two efforts at any one time and to try and work as an entire Committee rather than diffusing out into work groups because that did not seem to work as effectively. I think it would be important. We can begin to serve as a forum for the broad range of topics but that in terms of products, we should focus on one or at the most two at any point in time.

In terms of efforts to advance knowledge of genetic tests by the Department, assessment of these efforts to advance knowledge of clinical validity and utility of genetic tests in both premarket and postmarket phases includes analysis of projects supported by relevant DHHS agencies and primary research, secondary analyses, summary information development, and summary information dissemination, and this was quite an effort that was undertaken by staff, develop case studies illustrating the development of three genetic tests to learn more about how the genetics work together and with the private sector to advance the validation and integration of genetic tests.

Regarding education, it involved an exploration of educational challenges posed by expansion of genetic testing and the adequacy of efforts to prepare health professionals to use these new technologies appropriately, and we've heard discussion of that today, and we held a policy conference in May 2002 that identified the need for teaching and faculty development, training of geneticists and collaborative teams, funding for translational research, outcomes research, meaning evidence-based medicine, development of pedigree tools and data on the application of lab guidelines, and reimbursement patterns and codes.

Regarding access to genetic testing services, that involved an exploration of issues and access to genetic testing services, including coverage, billing and reimbursement of genetic testing services, and disparities in access to genetic testing services, and we held a town meeting on the accessibility of genetic testing services and to hear perspectives on how the problem should be addressed.

Additional topics under study, the importance of public understanding and the need for information materials on specific tests and categories of tests to reach disparate communities. A generic information brochure targeted to the general public was to be developed as a model. Conceptual framework, correlating test characteristics and approaches to informed consent in order to improve decisionmaking and the consent process in clinical and public health practice, and assessment of the translation, oversight, availability, and accessibility of genetic tests for rare diseases.

So with that as a summary, I'd be happy to take any questions for a couple of minutes.

DR. LEONARD: Can you tell me what the products of this Committee are supposed to be? Are they simply supposed to be recommendations for work that needs to be done or does this Committee actually do work and produce products that are usable in certain formats by the public or professionals? I need to understand what we're supposed to be doing, producing.

DR. McCABE: Well, that's what we're going to decide during the rest of the day. Let me give you some examples, though, from the SACGT.

I would include among our products, there was a white paper that was done that was prepared under contract early on to bring the group up to a similar database from which we proceeded to make the recommendations. That ended up being very popular on the website and we heard was used in education of undergrads and others. So I think that's an important product, if it was used in the educational process, but it was really intended as a document for the benefit of our group.

The other products included letters, the recommendation for support by the Administrations of genetic nondiscrimination legislation, and those were received favorably by both Administrations as well as the other letters that I mentioned. That's a direct way that we can directly communicate with the Secretary and give recommendations to the Secretary, and then there were the recommendations which were longer papers that established sort of the foundation for the recommendations and then went into the specific recommendations.

I think all of these are the kinds of products that we can have. I think the other more nebulous product is serving as a forum for discussion, but until that dogma in medicine and until it's written down, it doesn't exist, I think that just discussing something is nebulous. If we can then move from that discussion to something that is written and can be used in communication of the concerns, the issues, the priorities of this Committee, that I think that will have a lot more weight, but that's my own opinion and experience from before. I think it's important to have written products as well as the discussions.

DR. LEONARD: Thanks.

DR. McCABE: For example, Sarah was discussing with me this morning that a product that we could have would be the deliberations that we've had at this meeting, a laying out. It does not have to be a final recommendation, but it could be a discussion of the issues that have been laid before us and then a summarization of the discussions that will occur today because we've already begun to see some themes that have been brought up multiple times and just to put those down in written form and come to some document that we as a Committee could agree upon to move forward would be valuable.

DR. BEMENT: Did any of the products that came out of the previous Committee find its way into testimony or were they submitted as information for the record in testimony?

DR. McCABE: No, they did not, in terms of testimony before a legislative Committee, I assume you mean by that.

DR. BEMENT: That's what I mean, yes.

DR. McCABE: No, and we have to remember what our charter is, and we are a Committee of the Administration. We report to a cabinet-level Secretary. So that, our role is really to advise the Administration on these issues as laid out in our charter.

On one hand, in one case, however, I think it was the HELP Committee --

MS. CARR: The letter was used on the Senate floor, the poster.

DR. McCABE: Okay. The letter went to the Senate floor and was used there, but there was one time when, with the appropriate clearances, I think that some staff had some questions about some of the deliberations. So that, at one point, we did present to staff, and I think it was the HELP Committee but I could be wrong on that, but we had to have the appropriate clearances from the Secretary's office in order to do that.

DR. BEMENT: Right. No, I understood that and those caveats, but I'm just wondering if the Administration has seen the value of representing the work of the Committee to the Congress in that fashion, and I think you said in some cases, yes.

DR. McCABE: Yes. At least one of the products made its way to the floor and we're happy to provide guidance but that has to be with the appropriate clearance.

DR. BEMENT: Right.

DR. McCABE: And it's consultation. It's not really guidance. It's just our opinions.

Part of why that was requested was that we had been charged with public outreach, so we had also gotten a sense from the public, and we took that responsibility seriously, remembering that it was more than three years ago now, we were using Internet when it was in a much earlier stage to gather opinion.

Other questions or comments? Any comments from any of those of you who were involved with the SACGT?

DR.TUCKSON: I endorse what you said.

DR. McCABE: With that, thank you.

MS. MASNY: I know that you had already mentioned that the new Committee is not sort of a like a follow-up of the other Committee, but is there any way that we could make use of some of the information? Like for example, you have down that you were conducting the study on gene patents and had lots of discussion. Is there any way we could build on that as a foundation if we chose that as a priority area?

DR. McCABE: Yes. We didn't really conduct a study. We had a discussion at one of our meetings. We used that discussion. The Committee elected to use that discussion to recommend to the Secretary that there were health issues related to patents and licensure and recommend that those be considered. So I would assume that documents from the SACGT -- certainly the documents that were approved and moved forward are available.

What about the ones that were works in progress? Are they still available, Sarah?

MS. CARR: We can certainly share with the Committee the draft reports. In fact, we summarized the material in your briefing book and in the orientation book. I don't think in all cases we gave copies of the draft reports, more those that were farther along. I think the informed consent report is in there. But since they were draft and never approved by the Committee as a whole, they're not -- we don't post them

on the SACGT archives, for example. But I think the whole point of Ed's presentation was to bring this Committee up to date on what that Committee did and as a foundation for you to consider as you go forward and define priorities.

DR. TUCKSON: Ed, I would say, in terms of the work that was done from the last Committee, one body of that that was detailed, I thought, very good was on the analysis of clinical utility, validity, specificity of tests, and the oversight process. That is a really, really complicated and, quite frankly, painful. Unless you do it every day, it is a painful area.

We went through that in exhaustive detail, and I would say if anyone wanted a very complete but I think a good primer on how the process works for oversight of tests, how you decide whether a test is useful to go forward or not go forward, you can certainly speed up your knowledge base if you would take a look at those sections. I think it's written at a level that -- I'm not very bright and I think I kind of got it after awhile.

MR. MARGUS: Can I just ask, so when you say that we don't need to focus on that too much because it was done so exhaustively before?

DR. TUCKSON: Sir, I would never make that kind of statement on behalf of the Committee. What I do take from your question which I think is useful is that that's why I was sort of asking Dr. Sundwall from his testimony earlier, is given all the work that has gone on and at a point in time we saw it, and I think, Brad, what I don't understand is what's happened in the two years since that analysis was done, and that's what I sort of was looking for, was whether or not the way the world actually implemented these things, the way in which the FDA and the CDC and the CLIA actually got their hands around this, was it effective? Is it working or is it not? Brad, I don't know the answer to that.

MR. MARGUS: Can I also ask about the very last bullet you had, which was the last Committee assessed development of tests for rare diseases, and what was the consensus on that? I've heard a lot of anecdotal evidence, but was it the general consensus that it was inadequate and there needed to be more or what?

DR. McCABE: Let me first give you the context in which that work group was operating. We had seen data from GeneTests and there were other data as well. There was a paper published in JAMA by Peggy McGovern at Mount Sinai in New York, and the confluence of information was that if you looked at diseases for which there were genetic tests, the majority of diseases were actually rare diseases, which sort of fits with where we are in the history of genetics, that we're dealing with still the rarer "single gene" Mendelian traits, that a lot of those were being done in research laboratories.

This is a real problem for CLIA and for CMS as well. So there was a real concern about how to deal with this. How do you try and assure the public that they're having adequate oversight of rare disease testing without shutting it down and making it unavailable to a large group, a large population when you put it together collectively? So that's sort of where it was and it was a bit of a dilemma that the group was grappling with, but I don't think that work group had come to resolution.