***Public Comments***
**June 14, 2004**

DR. McCABE: Thank you.

With that, we now move onto the public comment. One of our critical functions is to serve as a public forum for deliberations on the broad range of human health and social issues raised by the development and use of genetic technologies. So we greatly value the input we receive from the public. We set aside time each day of our meeting to hear from the public, and we welcome and appreciate the views that you all share with us.

We also have received written comments that can be found in everyone's table folders. I would especially like to call your attention to several requests that additional time be provided to allow the public to comment on the draft documents being considered at this meeting.

In the interest of time, I ask our commentors to please keep your remarks to five minutes, if at all possible. Today we will be hearing from -- and I'll give this in order so you'll know when you're up -- Kathleen Rand Reed from the Rand Reed Group, Andrew Fawcett from the American Board of Genetic Counseling, and Barbara Handelin from Handelin Associates.

First, Kathleen. So please come up to the table, as Kathleen is doing.

MS. REED: Good afternoon. First of all, let me say thank you very much to Dr. McCabe for just a couple of more extra minutes, and I want to bring two issues to the record, and to the table.

I followed the bouncing ball, and that is I stuck to the priorities, and to the determinations such as overarching issues, and the priority short term, and the highest priority requiring in-depth study. The two comments that I would like to bring to the table, the first one would be continuing on genetic education and training of health professionals short term.

I am an anthropologist and an ethnomarketer, and I wanted to look at genetic issues that typically come into communities of color, especially those where the communities are what is known as hypersegregated. In other words, they are more than 95 percent of that particular group, because oftentimes in those particular communities, it is a little bit more difficult to get information and ask some of the questions. And yet, if they are to be served as well, then those are the kinds of communities to look at.

First of all, let me also say thank you to Joe McInerney, who was gracious enough in January to allow me to present a poster for the NCHPEG meeting. The title was a little bit controversial, but it was called "U.S. Prison Policies, the Baby Daddy, and Genetics in the Hood." Let me tell you the key components of the poster, and I think you'll understand why I said it is controversial, but it is critical that these issues are addressed.

The key components for the poster were one, the removal and incarceration of young black males from hypersegregated intercity neighborhoods and some rural towns, the high incidence of teenage mortality from violence, poverty, and poor health, the resulting skewing of the male to female ratio, the phenomena of multiple matings, which often result in high consanguinity levels, i.e. the baby daddy.

A review of cohorts born during the height of the war on drugs in 1990 to 1995, are currently on average reaching puberty in the years 2003 to 2008. The matings in many of these cases, because we have a member of the community that is often missing now, which is the gatekeeper, the genealogical gatekeeper, which is usually little old ladies that used to know who everybody was, and who belonged to whom.

Some of these matings may be between half-sibs, whose familial relationships may not be known within the general community. The potential is for possible epidemics of an increase in autosomal recessive disorders in this population, as well as a "blame the victim" mentality, and possible genetic redlining.

The reason I bring it to this particular group is because part of the comments that I got from the head of some of the genetic organizations, especially state-run, were chilling. They were chilling in this respect. As much as I was told that I was right, and in fact, I even had a deep conversation with Barbara Willis Harrison to get a reality check, to see if what I was thinking was absolutely true.

Ms. Harrison told me yes, we see this when I'm out doing pedigrees, this is a reality. And yet, one of the problems that we run into is this issue of genetics and the whole coming to terms with the community, and PC. What I found when I presented this poster, and I've had conversations with Mr. McInerney as well, is that many of the genetic counselors said yes, no, we see this in the pedigrees. The problem is because we are white, we can't do the PC part, because some people might think it is eugenics.

Now, I'm bringing these controversial issues. Anyone that knows me knows that I'm pretty much the one that always tries to bring up these kinds of issues, because some people don't, and I'm very comfortable doing this. But I would say that one of the things that we need to really work on, and this is an emergent situation, because I also went to Chicago, Detroit, Oakland, and Philadelphia and checked in and found that this is also a real big issue there, in many of the urban areas, and it is emerging.

I would say that we need to get on this and take a look. But one of the things that we need to do is create these bridges where we have deep conversations and issues around who is white, eugenics, and PC issues. As they say, get over it. We need to have deep conversations so that we can protect these communities. Let me move quickly, because I don't want to run out of time, but I throw that out there as an issue.

The second one is, and very quickly, you have already identified the diverse representation of the population in clinical trials has particular importance in genetic research, since genetic variation among populations may account for differences in disease prevalence, drug reactions, and susceptibility to environmental triggers, among others.

There is a problem. The problem is I just came back from California, spending time going back and forth and being an expert witness in several cases where minorities are now suing. They are becoming more sophisticated about genetics, and suing because they are having serious adverse events with regard to their pharmacogenetic reactions to various prescription drugs and their respective diseases.

They are beginning to sue both the institutions, the hospitals, the HMOs, their physicians, and the pharmaceutical manufacturers. In the case of minorities, often their primary care physicians are also minority physicians, and often these physicians rely on the details and warrants issued to them from the pharmaceutical manufacturers for their prescribing guidelines.

There is now a scientific gap, and a legal gap, that causes injury to both the minority patient, and in some cases, the minority physician. When a lawsuit of this type is filed, all parties are sued. The hospital, the HMO, the patients, physicians, and the pharmaceutical manufacturer. But the pharmaceutical manufacturers, however, have an automatic defense, namely the learned intermediary doctrine, or the LID.

The LID can best be described as the manufacturer owes no duty to warrant to the patient, but to the learned intermediary, i.e. the prescribing physician. The liability, if anything, rests with the physician, or the institution, for the prescription to the patient.

However, this learned intermediary doctrine has several caveats. Namely, the information given to the physician must be "adequate." You as a committee have already identified the the flaw in this process, where you say pharmacogenomics, page 2, paragraph 3. "The pharmaceutical industry has very little incentive to do pharmacogenomic studies on "already marketed drugs or generic drugs." Such studies are expensive, appear to offer no market advantage for the sponsor of the studies, and the identification of persons for whom the drugs would be ineffective, thereby creating a stratified market for their products."

This disconnect causes several downstream consequences. Number one, it

relieves the drug manufacturers of a look back, and the action with current information on pharmacogenomic information to offer not only adequate information to the learned intermediary, or the physician and the institution, but it also does not allow for the development of new information where minority participants were not included, and need to be included, and they need to have that look back.

From an ELSI perspective, this disconnect between the marketed drugs and revisiting old data, increases the discriminatory aspects which already face minority physicians, i.e. HMO's, and managed care. But it further reduces their numbers in the ranks, and to sum it up, this may wind up giving a look see also into some health disparities.

I would ask that you review these relationships, because the same relationships that occur with the drugs are going to be the same kind of relationships that you're going to experience when you look at pharmacogenomics and the genetic testing.

Thank you very much, and I hope that has been helpful.

DR. McCABE: Thank you very much, Dr. Reed.

Are there questions or comments?

MS. REED: That's Ms. Reed. Not quite doctor yet.

DR. McCABE: Questions or comments? Debra?

DR. LEONARD: So this type of look back is being done in Japan, where they are asking all pharmacogenetic analysis for drugs on the market be done for the Japanese population. Would you suggest that the federal government ask for this type of thing to be done in all the ethnic populations? Because it is not just African Americans, but Hispanics, and all the different ethnic groups in the U.S., and that would be a major effort, because we are so ethnically diverse.

MS. REED: I think it is the old expression, how do you eat an elephant? One bite at a time. I would think to go up against this, as you say, straight up, would be a problem. One of the things that I'm making a recommendation on, I sat on an IRB for Heart, Lung, and Blood at NIH, and one of the recommendations is that there is an easier way to do this.

When Hopkins had a problem with the literature search, and now people do real deep literature searches, because no one wants to be shut down anymore. There is so much of a proliferation of information now, until one of the things that I'm asking is that when you do your literature search, that you run out as one of your key words, the ethnic groups, just to get the information back and see if there is anything out there, and then you can incorporate that into your research design.

But I do think that there is a responsibility for some of the older drugs that have been out there. One on the new end to put the responsibility on the pharmaceutical manufacturer to do that kind of inclusive work, which they should be doing anyway, but to also on the older drugs, to begin to revamp and take a slow approach, but still take the responsibility of a look back.

DR. LEONARD: Maybe this could come, Joe Hackett, through the FDA with some sort of truth in labeling, such that for different medications, it has to be stated what ethnic populations it has been studied in, so that at least as part of what comes with a drug, you know that it has only been studied in Caucasians, or Caucasians and African Americans, or something like that, so that physicians have some ability to know the adverse reactions.
They may see adverse reactions in other populations in which the drug has not been tested.

MS. REED: And you are getting some of that in the DTC, in the direct-to-consumer advertising.

DR. HACKETT: My own perception is when you say that drug companies are very reluctant to do this, and we are trying to work with them on the newer drugs, it is all voluntary at this point. I can say again this year that there won't be any new diagnostic tests in using genomics this year, so it is slow.

MS. REED: At least it is on the table for you to examine. Thank you again.

DR. McCABE: Thank you, and I would point out that as we think about different ethnic communities, we need to think about genders, too, because that has been a problem in testing drugs as well. Thank you very much, Kathleen, for bringing that to our attention.

Next is Andy Fawcett from the American Board of Genetic Counseling. Andy?

MR. FAWCETT: I'm here today as a member of the Board of Directors of the American Board of Genetic Counseling. I'd like to begin by thanking the committee for allowing us this opportunity to provide comment.

The ABGC is a national accrediting and credentialing body of the profession of genetic counseling. The ABGC establishes minimum requirements for graduate programs in genetic counseling, and develops a criteria by which individuals become eligible to sit for the certification examination.

As this committee is well aware, genetics is one of the most rapidly advancing areas of scientific research, with clinical applications in practically all areas of medicine. The advances in medical genetics are forcing fundamental changes in the way health care providers practice medicine and think about health and disease.

Knowledge about genetics and its social and ethical implications is becoming increasingly essential for many health care professionals, and must become an integral part of their curriculum. The draft resolution on genetics education and training of health care professionals developed by this committee clearly recognizes this need, and makes several solid recommendations related to integrating genomic concepts into our health care system.

The ABGC, however, feels that it is critical that a distinct and separate focus on the education and training of genetics health care professionals be included in this resolution. As certified genetics professionals, we recognize that the demand for genetic counseling services will continue to increase, and unless more genetic counselors are trained, there will not be enough counselors to provide care to all patients and their families.

Many certified genetic counselors devote significant time and effort educating other health care providers. The primary objective of these endeavors is to teach these providers to recognize a genetic condition in a patient, handle more straightforward genetic issues, and develop a relationship with genetic professionals in their community as a resource upon which they may draw to provide optimal care to the patient.

This goal is not to teach other health care professionals to provide comprehensive genetic services. The issues surrounding genetic conditions are frequently complex, and as a result, a team of genetics professionals representing multiple genetic specialties may be required to provide this type of service.

For example, genetic counselors have unique and extensive training in human genetics and counseling skills. They take didactic course work in human, medical, and clinical genetics, counseling theories and techniques, bereavement, crisis intervention, cultural competency, social, ethical and legal issues related to the delivery of genetic services, health care delivery systems, principles of public health, teaching skills, and research methodology.

Genetic counseling programs accredited by the ABGC also provide extensive clinical training involving over 800 hours of field work, teaching, laboratory experience, as well as research. Genetic counselors are taught to prepare, deliver, and evaluate educational programs as they apply to various groups of learners. They are specifically qualified to deal not only with the complicated genetic and technical issues that often arise in the context of genetic evaluation counseling, but also the complex psychosocial, ethical, and legal issues with which patients and their families struggle.

Adequate financial resources must be in place so that an adequate number of individuals can be trained as genetic specialists. While the ABGC recognizes that educational efforts related to genetics must be aimed at our entire health care system, we encourage this

committee to acknowledge that equally important is support for the continued existence of health care professionals who have specialized training in genetics.

Genetics health care professionals, such as genetic counselors, have been, and will continue to be, the ones who train and educate other health care professionals about the many complexities of genomic medicine.

Seventy-seven percent of all genetic counselors are currently involved in the genetics education of physicians and medical students, according to a professional status survey administered by the National Society of Genetic Counselors in 2002.

One-third reported teaching genetics to other health care professionals. Many genetic counselors have developed and implemented innovative educational models that facilitate the genetics education of other health care professionals and students. They are also involved in forming public policy related to genetics, and actively participate in genetics education programs for the public.

The recommendations made by this committee to ensure that genetics education and training of all health care professionals is adequate, will only be successful if there is an adequate genetics workforce to implement these recommendations.

Currently, there are 1,811 certified genetic counselors, and 25 accredited genetic counseling programs, and graduate programs in the United States, and three programs in Canada. Of those who responded to the professional status survey referred to earlier, only 6 percent indicated they were non-Caucasian.

If genomic medicine is going to be equally accessible and practice in a culturally sensitive manner, individuals from minority populations must be recruited into the genetic counseling profession, and programs must be established in less populated areas of the United States.

In October of 2003, Robin Bennett, past president of the NSGC, presented data to this committee related to increasing the number and diversity of genetic counselors. To promote the training of genetic counselors, Ms. Bennett recommended that funding and granting opportunities be made available to support students and faculty in current genetic counseling programs, as well as to promote the establishment of new training programs.

The ABGC strongly supports the allocations of funds for this purpose if we are going to be successful in increasing the number and diversity of genetic counselors. Genetics health care professionals must reach out to other health care professionals to help them learn about the great promise and potential pitfalls of genomic medicine.

For this to be accomplished, we must ensure that there are competently trained genetics professionals. We strongly urge this committee to make specific and distinct recommendations to support the continued training of individuals in the field of genetic counseling, encourage increased diversity in our profession, and encourage those uniquely trained individuals to demonstrate their competency through certification and licensure.

Thank you.

DR. McCABE: Thank you, Andy.

Questions or comments for Mr. Fawcett? Yes, Debra?

DR. LEONARD: I think that this is an excellent point. We have often discussed in this committee the paucity of genetic counselors, and so I think this is sort of an oversight in our education resolution, and we may want to consider addressing this in some way.

DR. McCABE: Thank you.

Any other comments or questions?

(No response.)

DR. McCABE: Next we have Dr. Barbara Handelin from Handelin Associates.

DR. HANDELIN: Thank you, Dr. McCabe and members of the committee for allowing this additional opportunity to provide some comments on your excellent

deliberations, resolutions, and recommendations.

Let me just begin by saying that I'm here today principally representing myself as a Ph.D. geneticist who has been a technology developer and early practitioner of the provision of laboratory services and genetics in the commercial sector, as a consultant to large and small companies, and academic centers in the development of new genetic technologies and their implementation and practice.

I also speak from some 15 years of working with the IRB community in improving the oversight of genetics research involving human subjects, especially those that were sponsored by private industry.

I provided some written comments. I'm not going to reread those to you here today, but rather to move on to some additional thoughts that I have had in the meantime, in particular influenced by your conversations this morning.

I wanted to respond to the question that Brad Margus raised earlier about what may be broken, or is there something broken in the practice of medicine today with regards to genetics inclusion? I had the following thoughts.

While I'm routinely amazed by how often the genetic basis of a set of symptoms is not considered in a differential diagnosis, I also have to admit that I have an equal number of stories of people who have spent years of suffering and expense, failing to get a correct diagnoses, even when genetics is not involved. I know that all of us do.

I think that this is a reflection of the way we are perhaps not teaching physicians to think about a constellation of symptoms, about how to ask enough questions and hear enough answers about a patient's condition. But most importantly, how to think through a complex problem, considering many alternative diagnoses, as well as the physician being able to think about what is all the data that I'm going to need to collect in order to weave amongst those possible alternatives.

I would posit that perhaps this also says, most importantly, that we have far exceeded the capacity of the majority of physicians to keep a reasonably complete fund of knowledge of human disease in mind as they are seeing patients. Genetics are not.

In this vein, I would strongly support the idea that arose earlier today, I think originally by Dr. Tuckson, and then echoed by Sarah Carr about the timeliness of promoting the development and implementation of information technology systems that can support routine clinical practice, including the suggestion of genetic etiologies or contributions to common disease in everyday practice.

But I make this suggestion with a caution, and that being that these sort of practice tools have been developed previously and marketed by private companies, only to be rejected by many physicians because they don't like the feeling that a computer may appear to be doing my job. That kind of sense of pride in providing knowledge and experience is a barrier to the acceptance for such tools, and it causes me to wonder if perhaps we need to see some kind of requirement for such tools in large medical practices, in large institutions, or the requirement for such tools to be incorporated into new training programs.

So I'd also like to speak to several other points that were contained in the various briefs that the committee provides as background. In particular, I'd like to speak to the brief on large population studies. Genetics as a discipline, I learned when I was a Ph.D. student, is not the study of inherited traits, nor the study of inheritance itself, but rather more fundamentally, the study of variability. Variability in populations is sourced through inborn traits of a species. Variability in populations is the source of our biochemical patterns, our physiology, our response to infectious disease, to nutrition, in the form of allergies, for example, to exposure to xenobiologicals, plant toxins and venoms, to daily life stress, and to administer treatments, as in the case of pharmacogenetics.

Variability in populations is the source of our racial and other group traits, as we share specific variants with family members, and choose parenting partners within our close at

hand community groups. Variability in populations allows us to be at once a part of a group or sector, and to be individuals.

I would posit to the committee that the basic goals of our pursuit of knowledge about the human genome is fundamentally about understanding the variability in populations. Therefore, ensuring the potential to undertake such large population studies all across the United States through the various strata of our diverse population seems to me to be among the most important missions of all persons and committees who are charged with overseeing the exploration and application of genetic technologies in research and medicine.

So I hope that you here, and those at the NIH, and the NHGRI, for example, will focus on finding ways to list the main barriers to the ethical and productive conduct of large studies. I agree wholeheartedly with the observation made in the committee brief, that "the lack of the universal health care system, and the lack of a uniform electronic medical record system here in the U.S. are likely two very important barriers today."

The simple promise of guaranteed health insurance and health coverage, as are seen in other countries in the world, such as Sweden and Iceland, go a long way to encouraging people to participate in such large research protocols.

Other safety concerns for us is subjects, of course, about privacy and confidentiality. I would suggest that it has been now my conclusion I guess that we cannot ever guarantee absolute privacy, or that we could hold out all individual details completely confidential. Therefore, it seems paramount to me that we must feel confident that those who may choose to attempt to harm us through use of our private information will not be tolerated, that there will be severe consequences for such abuse of privacy.

I have an uncle who is an attorney who used to say that no one would cheat on their taxes if the death penalty were the required sentence. And so to be clear, while providing clear requirements for utilizing all the available methods for shielding private information from wrongful use, I believe it is equally important to develop a system of clear consequences for such wrongful acts, to send a message that as a society, we will not tolerate such violations of respect for persons.

In conclusion, I just want to say that I am using this language of respect for persons, which I take from the Belmont Report, one of the three general principles laid out by the Belmont Committee in the Protection for Research Subjects as a way to remind ourselves, again, that the reason that we have rules and regulations about the ethical use of human subjects arises from the misuse of genetic and other kinds of information here in the United States, and in Germany decades ago.

So I urge us to return to those simple principles, respect for persons, beneficence, and justice, as you continue in your important work here. The final point that I would like to take a minute to make is to applaud you on your thorough and thoughtful treatment on the reimbursement and coverage issues for new technologies, including those in genetics.

Since the first application of our knowledge of genes and performing carrier tests and prenatal predictive tests for single-gene disorders, we have been practicing a new kind of preventive medicine. I suggest that today, our nearest benefit from the genome knowledge base remains primarily in preventive medicine. As we see the very first of new cancer screening tests, first tests to identify patients who will or will not benefit from toxic chemotherapies, these are the kinds of new products that I think are going to typify the implementation of genetics in the next decade.

Therefore, I would especially encourage you to drive home the importance of creating a sea change in our coverage for preventive medical services, so that we can encourage to participate in the research necessary to get there, as well as in the enjoyment of those benefits.

Thank you very much.

DR. McCABE: Thank you, Dr. Handelin.

Any questions or comments, anyone?

(No response.)

DR. McCABE: Thank you very much.

I'm sorry. Emily.

DR. WINN-DEEN: I just had a question. How much do you think of the reason that genetics isn't considered is because physicians in their time constrained, by the clock office visits, are basically applying the 80/20 rule, where you take the most common diagnoses and sort of farm everybody through those, and just don't really have the time to consider the less likely scenarios, or the more infrequent scenarios?

DR. HANDELIN: Well, I guess I would question whether genetic etiologies, or genetic components of many common diseases are typically the uncommon explanations for many presenting symptoms. But I agree with you that certainly a reluctance to consider many other alternative diagnoses clearly falls principally from a lack of time right there in the office, as well as a lack of time to incorporate new ideas, new concepts, and new knowledge into your fund of knowledge. Again, I think it is pointing to the need for some assistance in doing that.

DR. McCABE: Any other questions or comments?

(No response.)

DR. McCABE: Thank you, Dr. Handelin.