

The American Society of Human Genetics

Policy Statement

ASHG Response to U.S. SACGT Request for Public Comments on Preliminary Recommendations on Oversight of Genetic Testing

May 22, 2000

U.S. Secretary's Advisory Committee on Genetic Testing
c/o Ms. Sarah Carr
National Institutes of Health
6000 Executive Blvd., Suite 302
Bethesda, MD 20892

Dear SACGT Committee Members:

The [American Society of Human Genetics \(ASHG\)](#) is the primary professional organization for human geneticists in North America. The ASHG represents over 6,700 researchers, physicians, laboratory professionals, genetic counselors, and others involved in the field of human genetics. ASHG members play a central role in various areas of genetics research and in the delivery of health care services derived from that research. On behalf of the ASHG Board of Directors, I am writing in response to the preliminary final recommendations in the April 19, 2000, U.S. Federal Register.

ASHG would like to express its appreciation for the work that the U.S. Secretary's Advisory Committee on Genetic Testing (SACGT) has done to produce a set of recommendations for Oversight of Genetic Testing as comprehensive and as far-reaching as these. To capture and address the public's concerns while incorporating the opinions of the scientific community, consumer groups and others into the document is remarkable.

Thank you for giving us another opportunity to comment. I will outline below some concerns and questions that members of the ASHG Board of Directors had after reviewing the recommendations.

Overarching Principles:

In general, the ASHG Board of Directors wholeheartedly supports the Overarching Principles.

Recommendations:

For the most part, there was general agreement on the five issues that the Committee addressed. However, throughout the document, two underlying questions are evident that determine the effect that some of the Committee's recommendations would have.

- 1.) It was not clear if the SACGT intends their recommendations to apply only to genetic tests that are offered commercially or also to tests done in the research setting. According to GeneTests, genetic tests currently exist for 743 conditions. However, clinical testing is available for only 419 of these, meaning that tests for another 324 diseases are offered only on a research basis. Since many of these diseases are quite rare, there may never be any interest in developing a commercial test for them. Moreover, because institutions may be unwilling to allow research laboratories that are not CLIA certified to release test results on individual patients, many patients at risk for rare diseases may never be able to derive any clinical benefit from research discoveries. This will be frustrating not only for patients and their families, but also for the genetics clinicians who work with them. We are concerned that families may become increasingly less willing to participate in research if they

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perceive that they and others confronting rare diseases for which commercial testing is unlikely to be profitable may not be able to be tested after the gene is characterized. We ask that the Committee clarify whether its recommendations are intended to apply just to commercial tests. If so, perhaps an alternative and less stringent mechanism of oversight than FDA review might be proposed that would allow "clinical" testing to be done by approved research laboratories if no commercial testing is available.

2.) From our perspective, there are problems with the definition of what exactly constitutes a "genetic test" that should require additional oversight. We suggest restricting the definition of genetic tests that would require additional oversight to those that test for a particular nucleotide sequence directly or indirectly. This would include all DNA and RNA testing, protein truncation and similar tests of expression that are based on DNA or RNA sequence, and FISH or equivalent kinds of molecular cytogenetic testing. While many genetic diseases can be diagnosed equally well by looking at a gene product, it appears that tests involving nucleotide sequence are the ones that generate particular concern among non-geneticist health professionals and the public, and it is this concern that justifies additional oversight.

Some ASHG Board members also had specific concerns about SACGT's recommendations for the following issues:

Issue 2 -- How can the criteria for assessing the benefits and risks of genetic tests be used to differentiate categories of tests? What are the categories and what kind of mechanism could be used to assign tests to the different categories?

The SACGT has done a good job of identifying several of the factors that affect the level of scrutiny to which tests should be subjected. However, as the Committee's later discussion reflects, this is an extremely complex issue, and one that we worry is perhaps oversimplified in the recommendations. We suggest that additional consideration be given to the dimensions that will determine the degree of oversight. Particular concerns were raised about weighting tests on the basis of the availability of an intervention or on features of the condition such as penetrance and prevalence. Clearly, the relative importance of these and other factors varies by condition, and each test will have to be considered on a case by case basis.

Issue 3 -- What process should be used to collect, evaluate, and disseminate data on single tests or groups of tests in each category?

ASHG Board members support the SACGT's recommendations that the responsibility for generating initial data on analytical and clinical validity of tests should rest with a test's developer. We also agree that longitudinal collection and dissemination of data on the clinical validity and utility of tests is essential. However, some members express concern that collecting long-term data on clinical validity and utility would place undue burden on academic laboratories.

Issue 4 -- What are the options for oversight of genetic tests and the advantages and disadvantages of each option?

It is generally agreed that special oversight of genetic testing is appropriate in light of societal fears about its misuse. However, at this point we do not know if these fears are warranted or not. It is conceivable that in 10 or 15 years genetic tests will be treated no differently than any other kind of medical test. The heightened oversight that is now perceived as necessary will raise the costs associated with these tests-costs that ultimately will be born by patients, providers, government agencies, and the general public. Therefore, we suggest that mechanisms for heightened oversight be provisional, with their effectiveness and necessity being reviewed every 5 years.

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The ASHG Board also has some concerns about the SACGT's recommendation that the FDA be the lead federal agency responsible for providing additional oversight. While in the past the FDA has always had the authority to act in this fashion, its purview has not included review of genetic tests based upon newly discovered disease genes. Specifically, the FDA has not reviewed or overseen so-called "home-brew" tests. As geneticists, we are concerned that too much regulation and oversight by the FDA-particularly at the time a disease gene has just been discovered and searches for mutations are still going on-might inhibit research.

Research laboratories discovering disease genes usually search the entire gene for mutations to begin elucidating genotype/phenotype correlations and to determine mutation frequencies in various populations. In order to do so, these research laboratories accept samples from many physicians. However, as stated above, research laboratories are usually not CLIA certified. If regulations were to preclude their reporting results on study participants back to referring physicians, it would be very difficult for such laboratories to obtain the number of samples needed to characterize the gene. The ASHG believes that IRB approval and informed consent should be sufficient for genetic testing at this stage of test development. Research laboratories usually continue testing as long as they can publish the results. Thereafter, many of these laboratories continue to offer testing, despite financial losses, because researchers feel committed to the community of patients with whom they have worked for many years to find the disease gene. If CLIA or FDA regulations eventually make it too cumbersome for these laboratories to continue offering this service, testing will no longer be available for affected individuals unless the test becomes commercially viable. This may never occur for tests for hundreds of rare genetic diseases.

Additional Recommendations:

While the Committee has addressed the critical need for access to appropriate genetic education and counseling for genetic testing, no mechanism is suggested for how or at whose expense this would happen. Genetic evaluation and counseling are essential in order to ensure (1) that patients have an opportunity to consider the pros and cons of testing thoughtfully, (2) that the right genetic tests are done, and (3) that the results are interpreted correctly. While it is important to encourage the incorporation of more genetics into medical, nursing and allied health professional education, it is unrealistic to expect these providers to attain the same level of expertise as geneticists. We would like to see the Committee's report recommend additional support of training programs in clinical genetics and genetic counseling and appropriate reimbursement for genetics services to assure that this expertise continues to be available.

In conclusion, as the SACGT completes its task, we ask it to bear in mind that any regulatory changes must not undermine further research required for understanding and developing treatments for disease-particularly rare genetic diseases. It is also critical that oversight of genetic testing be sufficiently flexible to ensure continued participation in research by patients and the scientific community. Finally, I would like to reiterate that any regimen for heightened oversight of genetic testing should be provisional and re-examined every 5 years. Societal and scientific changes are occurring rapidly in this area, and what is appropriate today may require revision as our knowledge of the genetic contribution to human diseases increases.

Sincerely yours,

Ronald Worton, PhD
President, ASHG