CDC Genetic Forum - Laboratory Workgroup
Summary of Meeting
June 2, 2000
Atlanta, Georgia

1. Welcome and Introductions

Dr. Baker welcomed the workgroup and thanked for them for participating in this the first working meeting of the Laboratory Forum. He reminded participants of the three primary purposes of the Forum including: 1) to provide a venue for dialogue; 2) to provide an opportunity to develop a consensus on laboratory-related genetic issues and to channel advice to government agencies and advisory committees; and 3) to provide a mechanism to coordinate and collaborate on laboratory-related genetic educational issues.

2. Review of February 23, 2000 Forum meeting

Dr. Martin reviewed the February 23, 2000 Forum meeting, describing why the Forum was formed - as a result of both encouragement of Dr. McCabe, the Chair of the SACGT, for organizations to work together on issues, and to meet the ongoing concerns raised by CLIAC . He described the agreements about the operation of the Forum that had been reached during the first Forum meeting and his presentation to the SACGT on February 24, 2000. The Forum was described as a place to help define the nature and extent of contributions that can be made by professional organizations, government, and industry individually and collectively to help resolve laboratory-related genetic testing issues.

3. Gene Patenting

Drs. Popovich and Watson described some important implications of the recent surge in patenting of genes. Gene patenting could have the effect of reducing the number of laboratories offering specific genetic testing services, which would decrease the efficiency of proficiency testing (PT) programs and could eliminate the opportunity for PT for some genetic tests. It would also prove more difficult to exchange samples between laboratories to validate test accuracy. A test monopoly could lead to increased costs for genetic testing services and could decrease innovation in the field. In response, the American College of Medical Genetics (ACMG) and others are questioning whether human genes should be subject to patenting, since they are part of the naturally occurring essence of human existence. Some feel that no exclusive patents should be granted, since this could limit access to testing, increase costs, and decrease the drive for service quality that is promoted by market competition. They are attempting to engage the public in the debate. Canavan's disease was described as an example of how a monopoly might affect the delivery of genetic testing services. Members were

reminded of the Patent and Technology Office's public comment solicitation on this issue and the upcoming presentation of the gene patenting topic to the SACGT. The fundamental societal issue is what aspects of genetic testing should be subject to being patented?

Discussion followed about what the Forum might be able to contribute on this issue, with Dr. Baker indicating that it could: 1) enhance the science base by providing case studies to help guide public policy; 2) document changes in the quality of test service resulting from gene patenting; and 3) provide other options to maintain access and quality. A recommendation was made by one participant to consider presenting the gene patenting issue, with supporting data to the National Bioethics Advisory Commission (NBAC). Dr. Charache thought that the Forum could help by defining the attributes of quality in genetic testing that arise from having testing performed at multiple sites and by supporting the maturation of genetic testing by bringing the laboratory and medically oriented groups together to consider how tests should be integrated into clinical and public health practice.

4. Reimbursement for genetic tests

Drs. Watson and Popovich indicated that inadequate reimbursement for genetic testing was a growing concern, with Medicare reimbursement covering only about 20% of actual operational costs and with most university hospitals losing money. Third party payers may have their own reimbursement policies. Each mode of payment could constrain adding new services or improving existing offerings. Adoption of certain provisions of the genetics Notice of Intent could make the situation worse by adding new operational costs. The inadequacy of the five HCFA CPT codes for molecular diagnostic tests, which were developed in the 1980s, to address today's testing conditions was highlighted. The presenters indicated that there is a real need for HCFA or some other group to conduct a cost analysis to reassess the costs of service provision and change the amount of reimbursement for genetic tests. This study should take into account the new costs for providing services including payment of patent royalties. It should also account for the cascade effect of having a specimen that must be sent to several different laboratories for analysis, with each laboratory performing only a portion the genetic tests requested.

It was pointed out that every new Federal regulation must be accompanied by an impact analysis, which estimates the costs that might be incurred as a result of implementation of new laboratory requirements. An additional component that should be considered in reimbursement of genetic services is the educational cost required to assist the user of genetic services with test selection and result interpretation.

5. Notice of Intent - Genetic testing under CLIA

Dr. Boone presented an overview of the Clinical Laboratory Improvement Advisory Committee (CLIAC) recommendations published in the May 4, 2000 *Federal Register* CLIA Notice of Intent (NOI). He reviewed the major issues about which questions are being asked and urged the Forum members and the organizations they are members of to submit comments by the July3, 2000 due date.

Discussion centered on the definition of the genetic specialty, clinical validity, informed consent, confidentiality, and genetic counseling. Of interest to the group were: 1) whether newborn screening should be treated as a special category or not; 2) whether the care provider was primarily responsible for obtaining informed consent; 3) whether a genetic counselor had to be located in the laboratory performing the genetic test; 4) whether heritable and acquired diseases or conditions should be treated differently, since analytical validity was the primary concern with tests for acquired conditions. It was pointed out that CLIAC has supported the concept of making decisions about the application of CLIA requirements on a test by test basis. An effort will be made to analyze the comments to the NOI before the next Forum, CLIAC, and SACGT meetings. Based on comments to the NOI, the CLIAC could offer additional recommendations. Current plans are to develop a Notice of Proposed Rule Making in 2001 and a final rule in 2002.

6. New York State Oversight of Genetic Testing

Dr. Aviles-Caggana reviewed the extent and nature of oversight of genetic testing laboratories in New York State. She indicated that provider compliance with informed consent was poor, but laboratories were required to make a good faith effort to document that informed consent had been obtained. Funding for genetic counselors was not provided. Laboratory claims of analytical validity were reviewed along with requisition forms. Laboratories were required to perform split sample verification. Laboratory test result reports were examined to determine if they contained usable information. New York provides an orphan test exemption. Reviews of claims must be completed in 6 weeks and fees are charged based on test volume. Fees cover the costs of on-site inspection of the laboratory and of the review of claims and other information mentioned above.

7. A genetic testing framework - Discussion of National Genetic Testing Assessment Program (GenTAP)

Drs. Khoury and Boone presented a model framework for collecting and analyzing the data that are needed to assess the status of genetic testing at any point in time. GenTAP would help determine what we know and don't know about a test's analytical and clinical validity and clinical utility. The model

includes a review of laboratory claims, which would be assembled into a data base. Information in this data base could be combined with data from public health and clinical surveillance data to assess the clinical validity and utility of genetic testing for specific diseases or conditions. In turn, these data could be used for a comprehensive technology assessment to determine whether national screening programs or other interventions might be appropriate for a disease or condition. The first step in this process would be to develop a template for the data and information that would need to be collected to perform assessments. The Forum was asked whether this model seemed workable and whether criteria could be developed to help form the template for data collection.

Topics raised during discussion included: 1) individual laboratories could have a difficult time establishing clinical validity without a framework such as the one proposed; 2) if laboratory claims are rejected as being inadequate to be included in the database, whether some tests might never accumulate sufficient clinical data to determine clinical validity; 3) whether marketed and in-house developed tests should be treated differently; 4) that the intended use of the test should be taken into account when considering clinical validity; 5) whether other laboratories should be allowed to base its claims for analytical and clinical validity on a test that was developed by another laboratory whose claims had been substantiated; 6) whether high and low prevalence conditions should have different criteria for clinical validity; 7) whether initially only a test's analytical reliability should be considered, so that tests using equivalent technologies might be more easily evaluated; 8) that the Forum would be a good place to develop criteria for the laboratory portion of GenTAP; 9) whether GenTAP could not only serve as a data repository, but also a specimen repository; and 10) whether university research laboratories should be treated differently in the system (education institutional costs and orphan test cosiderations) . In addition, the group attempted to clarify how much difference it would make if the threshold for acceptable data was set low initially and who would determine what was acceptable. Tests are being implemented very rapidly after a publication and concern was expressed about the speed at which decisions about test acceptability could be made in order to rapidly incorporate new technology. After considerable discussion, the group decided that it was an appropriate body to develop criteria for specific categories of genetic tests (NCCLS was mentioned as a possible alternative, but several questioned whether a product could be developed in a timely manner by NCCLS). They group then addressed the need to see how well the model might work for specific genetic test categories.

8. Development of Criteria and Action Items

The group decided to begin developing criteria for GenTAP by considering the categories of genetic tests by the purpose for the test, using the categories included in the SACGT's April 12, 2000 preliminary report, but adding a category called orphan testing. They also decided to start with heritable diseases.

For each category a heritable disease or condition was to be selected for which to develop criteria as follows:

Diagnostic/confirmatory testing - Fragile X, Cystic Fibrosis, Factor V Leiden
Predictive testing – Breast cancer (BRCA1 and 2)
Presymptomatic testing - Huntington's disease
Carrier testing - Cystic Fibrosis
Prenatal - Cystic Fibrosis
Orphan testing - Marfan's Syndrome
Preimplantation diagnosis - ?
Newborn screening - Cystic Fibrosis

Action Items -

1. Drs. Watson, Noll, and Winn-Deen volunteered to look at the categories and example diseases or conditions listed above and develop specific criteria might be applicable. This would help, construct the template that would describe the boxes that need to be filled in for GenTAP and see if the overall model is workable.

2. Drs. Popovich and Khoury were to develop the clinical criteria for the template using these same categories and diseases.

3. The CDC was to assemble the criteria being used by various government agencies and professional organizations to evaluate the analytic validity, clinical validity, clinical utility, and other features of genetic tests.

4. The CDC will look for a date and location for the next Forum meeting. This date should be before the next SACGT and CLIAC meeting, if possible, which means an early August date is most likely.

Summary

1. The Forum could serve as mechanism to review scientific evidence of any presumed harmful effects of gene patenting or of test reimbursement policies. It could also help develop specific recommendations for changing existing government policies for the SACGT and CLIAC or to present directly to the government agency responsible for oversight.

2. The Forum agreed that the determination of what we know and don't know about a genetic test would be useful. However, whatever process is developed to make these assessments must be flexible, responsive, timely, efficient, and easily updated as new information is generated. The Forum wants to explore the possibility of using something like GenTAP in

conjunction with professional organization, government, and industry to see if a workable process can be developed.

3. The next Forum meeting was tentatively scheduled for August/September 2000.

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