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Oversight of Genetic Testing

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As gene discoveries continue to emerge from the Human Genome Project, the number of genetic tests will grow exponentially. Currently, there are tests available for over 900 diseases/conditions in more than 500 laboratories (GeneTests-GeneClinics, 2001). These tests provide opportunities for health promotion and disease prevention; however, their sensitive nature has prompted organizations to call for regulation of genetic tests. Federal and State governments, as well as professional societies, have become involved in the regulation and oversight of genetic testing laboratories.

Definition of Genetic Test. The types of tests included in the definition of a genetic test vary. Several definitions of a genetic test can be found in existing state legislation and proposed Federal legislation. The term can refer to only DNA-based tests, or it can include tests of gene products, such as proteins and metabolites, chromosomes and even acquired somatic cell mutations such as those associated with cancer.

Genetic Testing Issues. Certain characteristics of mutations and genes make their analysis complex: one gene may be associated with more than one disease; a disease may be caused by mutations in more than one gene; and one gene may alter expression of another gene. In addition, the presence of a mutation may not necessarily result in a disease or condition. Other issues to consider are: the method and type of testing; the purpose of the test; the validity of the test, the authorization to order a genetic test; the entities responsible for informed consent; the laboratory personnel requirements; and the regulatory requirements for different types of laboratories.

Current Regulatory Environment

Regulation can take several forms, including licensing of laboratories and their personnel, proficiency testing, and quality assurance/quality control programs. The responsibility of genetic test oversight falls to several Federal agencies. At the Federal level, genetic tests are regulated by the Clinical Laboratory Improvement Amendment of 1988 (CLIA) regulations, the Federal Food, Drug and Cosmetic Act, and the Federal Policy for the Protection of Human Subjects during investigational phases. A few states also have taken initiative in establishing regulatory guidelines. Other forms of laboratory oversight may involve voluntary adherence to professional guidelines or best practices.

Clinical Laboratory Improvement Amendment. While genetic testing laboratories are subject to CLIA, the amendments offer no genetic-specific regulations other than the cytogenetics specialty, resulting in limited evaluation and quality assurance oversight (SACGT, 2000). However, the Clinical Laboratory Improvement Advisory Committee (CLIAC) is in the process of forming recommendations for a genetic testing specialty within CLIA. Washington and New York are exempt from CLIA and conduct their own lab inspections, because they have state standards more stringent than CLIA.

Food and Drug Administration. The FDA regulates laboratory tests as diagnostic devices; thus, tests sold as kits are subject to FDA approval. However, most genetic tests are developed in-house at laboratories (“home-brew”) and are provided as clinical laboratory services. The FDA has established regulations for the active ingredients used to perform these “home-brew” tests known as analyte specific reagents (ASRs) if produced

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by certified good manufacturing practices (GMP) vendors. The FDA is developing a template for reviewing laboratory specific home brewed genetic tests as recommended by the Secretary's Advisory Committee on Genetic Testing (SACGT).

Secretary's Advisory Committee on Genetic Testing. The SACGT was formed by Secretary of the Department of Health and Human Services (HHS) in June 1998. The SACGT is charged with advising HHS about all aspects of the development and use of genetic tests, including the complex medical, ethical, legal, and social issues raised by genetic testing. The SACGT has produced several reports, including "Enhancing the Oversight of Genetic Tests" and continues to develop recommendations for the current Secretary.

Centers for Medicare and Medicaid Services (CMS) is responsible for implementation of CLIA and the CLIA standards. CMS has regulatory authority for all laboratory testing. CDC is responsible for test categorization.

CDC's National Center for Environmental Health (NCEH) offers the Newborn Screening Quality Assurance Program, a voluntary, non-regulatory program to help State health agencies and their laboratories maintain and enhance the quality of test results. This program is offered in partnership with the Association of Public Health Laboratories.

State Initiatives. New York is the only state that has drafted specific laboratory practice standards for cytogenetics, biochemical and DNA based genetic testing, and molecular oncology for somatic mutations. New York's Clinical Laboratory Evaluation Program (CLEP), monitors the quality of tests conducted by all clinical laboratories and blood banks throughout the state, as well as out-of-state laboratories that accept specimens obtained in New York. CLEP issues laboratory permits and conducts a proficiency testing program which currently includes the category of cytogenetics and molecular oncology. California and Nebraska also have addressed the issue of regulation.

Role of Professional Societies and Private Sector. Professional societies and private organizations have become involved in the development of guidelines for genetic tests. For example:

- Association of Public Health Laboratories examines the impact of regulations and oversight on state newborn screening programs and the role of public health laboratories in the oversight of genetic tests.
- American College of Medical Genetics has developed guidelines for the use of particular tests and test methodologies.
- College of American Pathologists develops standards for its membership and operates a proficiency testing program.
- National Committee on Clinical Laboratory Standards develops consensus standards for test methodologies.
- Commission on Office Laboratory Accreditation offers a laboratory accreditation program.

Summary

The regulation and oversight of genetic tests will need to emphasize Federal interagency coordination and work in tandem with the states and professional societies. Regulations will need to be forward-thinking and periodically reviewed, as developments in technology, such as fluorescence *in situ* hybridization (FISH), tandem mass spectrometry and DNA microchip testing, continue to change the landscape of genetic testing.

Selected References

GeneTests-GeneClinics Home Page. 20 December 2001. <<http://www.genetests.org/>>.
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