

Policy Brief: CLIA and Genetic Testing

The federal government has a long history of overseeing clinical laboratories. Congress enacted the Clinical Laboratory Improvement Act in 1967 (CLIA '67), following testimony regarding the high error rate in laboratory testing. CLIA '67 was limited in scope. In the late 1980s, Congressional investigations found significant problems in the quality of testing services being provided to the public. Many laboratories were not subject to the federal regulations then in place, and many of those laboratories that were subject to the law were not complying with its requirements. The major problems identified by Congress were "lax federal oversight and direction, lack of proficiency testing for many analytes, inconsistent criteria for acceptable laboratory performance, and improprieties by laboratories in handling specimen samples."¹

Deficiencies were particularly apparent in cytological screening of pap smears for cervical cancer. Congress found that many laboratories were reporting false negative results. In response, Congress enacted the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88 or CLIA).

CLIA requires the Department of Health and Human Services (HHS) to issue standards for laboratory certification that will ensure that laboratories consistently perform tests in a valid and reliable manner. These standards must include the laboratory's maintenance of a quality assurance and quality control program; maintenance of appropriate records; equipment and facilities requirements; adherence to personnel standards; and compliance with proficiency testing requirements.

Regulations implementing CLIA first went into effect in 1992. The regulations categorize laboratory tests by complexity level, and specify different requirements depending on the level of complexity of the test performed. Tests are categorized as either waived, moderate complexity, or high complexity. Labs performing tests of moderate and/or high complexity must, in addition to general registration and inspection requirements, comply with applicable proficiency testing, patient test management, quality control, personnel, and quality assurance provisions of the regulations. Also, they must apply for certification for each testing specialty or subspecialty for which certification is sought.

Proficiency testing, i.e., "a method of externally validating the level of a laboratory's performance,"² was a key element of CLIA. According to the legislative history, Congress believed that proficiency testing "should be the central element in determining a laboratory's competence, since it purports to measure actual test outcomes rather than merely gauging the potential for accurate outcomes."³ Congress intended for HHS to develop "more rigorous standards than have heretofore been applicable."⁴ Authority to implement CLIA was delegated to the Center for Medicare and Medicaid Services (CMS).

BOARD OF DIRECTORS

President

Edward Abrahams, Ph.D.

Chair

William S. Dalton, Ph.D., M.D.
M2Gen

Vice Chair

Stephen L. Eck, M.D., Ph.D.
Astellas Pharma Global Development

Treasurer

D. Stafford O'Kelly
Abbott Molecular Inc. (Ret.)

Secretary

Amy P. Abernethy, M.D., Ph.D.
Duke University Medical Center

Past President & Chair

J. Brian Munroe
Endo Pharmaceuticals

Past Chair

Wayne A. Rosenkrans, Jr., Ph.D.
MIT (Ret.)

Steven Averbuch, M.D.
Bristol-Myers Squibb

Patrick J. Balthrop
Luminex Corporation

Paul R. Billings, M.D., Ph.D.
Thermo Fisher Scientific

Jeffrey Cossman, M.D.
United States Diagnostic Standard
(USDS)

Neil de Crescenzo
Emdeon Inc.

Donna Cryer, J.D.
Global Liver Institute

Felix W. Frueh, Ph.D.
Opus Three LLC

Tim Garnett, FRCOG, MFFP, FFPM
Eli Lilly and Company

Julie K. Goonewardene
Member, Board of Trustees,
American Medical Association

Michael Kolodziej, M.D.
Aetna

Lawrence J. Lesko, Ph.D., F.C.P.
University of Florida

*Aidan Power, M.B.B.Ch., M.Sc.,
M.R.C Psych.*
Pfizer Worldwide Research and
Development

Lori M. Reilly, Esq.
PhRMA

Jared N. Schwartz, M.D., Ph.D.
Leica Biosystems

Michael Vasconcelles, M.D.
Millennium: The Takeda
Oncology Company

Jay G. Wohlgemuth, M.D.
Quest Diagnostics

The regulations require laboratories performing moderate or high complexity tests to enroll in a CMS-approved proficiency testing program for each specialty or subspecialty for which certification is sought. Samples used in proficiency testing must be tested in the same manner as patients' specimens. Labs are judged by how well they are able to accurately perform the test at issue. The regulations establish the test score that the lab must receive for each specialty and subspecialty. Laboratories that do not successfully participate in proficiency testing are subject to sanctions, including suspension or revocation of certification.

CLIA and Genetic Testing

Genetic tests are considered high complexity tests under CLIA regulations. However, with the exception of cytogenetics, there is no specialty area covering genetic testing laboratories, and therefore no specified proficiency testing requirements. CLIA regulations serve as a baseline, i.e., a minimum standard to which all clinical laboratories must adhere to. Many laboratories go far beyond the CLIA minimum through voluntary accreditation programs. For these laboratories, an appropriately crafted genetic testing specialty would not add new burdens.

In the mid-1990s, key federal agencies began to take note of the growing use of genetic tests in clinical practice, and raised concerns about the adequacy of oversight for both genetic tests and the laboratories that develop and perform them. In 1997, a joint task force of the National Institutes of Health (NIH) and the Department of Energy (DOE) issued several recommendations to improve the quality of genetic testing, including a recommendation for enhanced regulation of genetic testing laboratories.⁵ Subsequently, an advisory committee to the Centers for Disease Control (CDC) recommended that the regulation of clinical laboratories be amended to include a genetic testing specialty area. In May 2000, these recommendations were published in the Federal Register for public comment as a Notice of Intent (NOI), with the statement that CMS would issue a proposed rule based on comments received.⁶ The NOI noted that, along with the "tremendous potential for improving health and preventing disease, genetic testing can also do great harm" if errors occur in test selection, performance, or interpretation.⁷ The NOI cited literature pointing to errors or substandard practice in each of these categories.

An analysis of the 57 comments received in response to the NOI reveals broad consensus regarding the need for a specialty area for genetic testing to ensure quality.⁸ While there were concerns about some of the ancillary recommendations of the NOI, e.g., those regarding informed consent and counseling, there was widespread agreement that the creation of a genetic testing specialty would improve the safety, accuracy, and reliability of genetic testing.

A diverse array of stakeholders has already raised its voice in support of a genetic testing specialty under CLIA, including nearly 100 representatives from patient, industry, health care provider, and women's health organizations.⁹ While the agency has recently placed the issuance of a Notice of Proposed Rulemaking (NPRM) on its semi-annual regulatory agenda,¹⁰ there can be no certainty that the agency will issue the NPRM, or that it will expeditiously finalize rulemaking once the NPRM has been issued.

Why a Specialty Area is Needed

Today, there are genetic tests clinically available for close to 1,000 diseases, and several hundred tests are in development, making genetic testing the fastest growing area of laboratory diagnostics. Genetic testing is becoming an increasing part of medical care, and is used in screening, diagnosis, treatment, and prevention. Pharmacogenetics promises to open up a new frontier in medicine by allowing the development and labeling of drugs based on knowledge of individual genetic variation, thereby increasing safety and efficacy. But the success of pharmacogenetics is predicated on the development and availability of genetic tests that accurately and reliably predict a patient's response to a drug. Put simply, to realize the promise of pharmacogenetics, physicians, patients, the pharmaceutical industry, and payors must have confidence in the accuracy and reliability of genetic testing.

Recent data to be published by the Genetics and Public Policy Center reveals a strong correlation between performance of proficiency testing and test quality. A survey of laboratory directors of genetic testing laboratories indicates that the more proficiency testing a laboratory performs the fewer deficiencies and analytical errors it reports. These data also indicate widespread support in the laboratory community for a genetic testing specialty under CLIA.

Support for a genetic testing specialty is consistent with PMC's stated goal of removing barriers to the success of personalized medicine. By supporting a specialty, PMC has an opportunity to concretely demonstrate its commitment to quality genetic tests.

1 H.R. Rep. No. 100-899 at 16 (1988).

2 Id. at 15.

3 Id. at 27.

4 Id. at 30.

5 Promoting Safe and Effective Genetic Testing in the United States: Final Report of the Task Force on Genetic Testing (Neil A. Holtzman and Michael S. Watson eds., 1997).

6 65 Fed. Reg. 25928 (May 4, 2000).

7 Id. at 25929.

8 Murphy, J., Javitt, G., Hudson, J. Creating a Genetic Testing Specialty Under CLIA: What Are We Waiting For? November 29, 2005, available at <http://www.dnapolicy.org/resources/McClellanpaper.pdf>.

9 See <http://www.rhfp.org/documents/CLIAlettertoCMSecMcClellan.pdf>; http://www.geneticalliance.org/ws_display.asp?filter=testing_ltr.

10 71 Fed. Reg. 22537, 22595 (Apr. 24, 2006).