



Advancing Excellence

**College of American Pathologists
Statement to the
Clinical Laboratory Improvement Advisory Committee (CLIA)**

**Presented by
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Dr. Sundwall, members of the committee, good afternoon. My name is Debra Leonard and I am an Associate Professor of Pathology and Laboratory Medicine and Director of the Molecular Pathology Laboratory at the Hospital of the University of Pennsylvania. I direct the Molecular Pathology Laboratory that performs molecular testing for genetic diseases, infectious diseases and cancers. I currently serve as a member of the Department of Health and Human Services Secretary's Advisory Committee on Genetics, Health and Society (SACGHS) and am a past President of the Association for Molecular Pathology. Today I am here as a representative of the College of American Pathologists (CAP). I am a member of the CAP Molecular Pathology Resource Committee, and served as chair for a Molecular Test Validation Project Work Group of which I will provide further details in my remarks.

The CAP is a national medical specialty society representing over 16,000 pathologists who practice anatomic pathology and laboratory medicine in the United States and Canada. The College's Commission on Laboratory Accreditation is responsible for the accreditation of over 6,000 laboratories worldwide. College members have extensive expertise in providing laboratory services and serve as inspectors in the accreditation program. In addition, the CAP provides laboratories with a wide array of proficiency testing and educational programs to assist in the improvement of the laboratory's performance and its positive impact on patient care.

The comments expressed by the CAP reflect a set of fundamental principles regarding genetic testing and the quality of laboratory medicine. The process used to develop the CAP position on genetic testing has been thorough and thoughtful. Experts in pathology and molecular pathology on the CAP Molecular Pathology Committee and the joint CAP/American College of Medical Genetics Biochemical and Molecular Resources Committee have analyzed and discussed the issue at length. Thus, the CAP policy has been developed with advice from genetic testing experts.

The purpose of my remarks today is to provide the Committee with a brief summary of the CAP's approach to addressing genetic testing oversight utilizing existing regulatory mechanisms, accreditation and proficiency testing programs. In May 2002, the CAP presented a "Conceptual Framework for Genetic Testing Oversight" to participants at the FDA Professional Roundtable meeting. This approach was designed to encourage the introduction of new genetic tests, and thus recommended utilizing the existing CLIA laboratory inspection and accreditation process to provide oversight and approval of genetic testing in lieu of new federal regulations. The message that the CAP communicated, with the general consensus of those at the meeting, is that the existing CAP/CLIA inspection and accreditation program can be built upon to satisfy the concerns surrounding genetic tests. The purpose of our testimony is to provide some background on our approach and provide you with our progress to date.

The CAP "Conceptual Framework for Genetic Testing Oversight" consists of three primary components:

- **Review of Laboratory-Developed Test Validation;**
- **Inspection by Inspectors with Genetic Testing Experience; and**
- **Availability of Proficiency Testing Programs for Genetic Tests**

1. Review of Laboratory-Developed Test Validation

The CAP's first goal was to provide a mechanism within the inspection process for the review of genetic tests developed by the laboratory without the use of FDA approved test kits. The goal is to ensure that every genetic test is analytically sound and has been properly evaluated and appropriately labeled. The intention is to provide the additional oversight in the existing inspection and accreditation process that was to be provided by the new FDA review process.

The CAP has drafted a new section of the Molecular Pathology Laboratory Inspection Checklist to address genetic test validation. The draft includes ten new checklist questions and commentaries, drawn largely from the FDA's Test Review Template, and

addressing issues of analytical validity, clinical validity and appropriate reporting. Specifically, the clinical validity of the test can be documented through either literature citations or internal studies. The new questions will apply to all laboratory-developed molecular tests introduced since the last inspection. The new checklist questions are currently under consideration by the CAP Commission on Laboratory Accreditation. It is expected that they will be approved and incorporated into the Molecular Pathology Checklist by the end of 2003.

2. Inspection by Inspectors with Genetic Testing Experience

The second goal of the CAP is to assure that qualified inspectors are used to inspect genetic testing laboratories. The CAP has a growing list of qualified inspectors available to join on-site inspection teams for specific specialty areas, including Cytogenetics, Biochemical and Molecular Genetics and Molecular Pathology. Current recruitment efforts include a request for information on the specific relevant experience of potential specialty inspectors, as well as inspector-training sessions at relevant professional meetings. In the past two years, the CAP has co-sponsored laboratory inspector training seminars with the American College of Medical Genetics (ACMG) and the Association for Molecular Pathology (AMP). These events yielded close to 200 new specialty inspectors. The College's efforts are in direct concordance with current CLIA regulations specifying the qualifications, education, and experience requirements for inspectors, as well as the availability of training programs for inspectors.

3. Availability of Proficiency Testing Programs for Genetic Tests

The third goal is to enhance the existing Proficiency Testing Programs of the CAP for genetic tests. The CAP recognizes the value of Interlaboratory Comparison Programs for genetic testing in providing checks for laboratory test quality. Proficiency testing can identify poor test performance and allow for corrective action even when internal comparisons are consistent over time (good precision/poor accuracy). Moreover, comparative statistics across a testing program may detect biases between different

instruments, reagents, and techniques. The CAP believes these statistics would objectively reflect the current state of laboratory practice, as opposed to arbitrary standards set by outside agencies. The CAP recognizes that genetic proficiency testing programs must cover a wider menu of genetic disorders and include more challenges. New proficiency testing models are being considered for those genetic tests performed in just a few laboratories. Laboratories have expressed interest in having this type of proficiency testing program available; however, high costs remain a challenge for potential participants.

As a Centers for Medicare and Medicaid Services (CMS) recognized accreditation body, the CAP has been operating a program of onsite inspection and proficiency testing founded upon compliance with established performance standards, professional peer review, and education. The CAP joined with the American Society of Human Genetics, and the American College of Medical Genetics, specifically to develop performance standards and proficiency testing programs, including standards for the validation of laboratory developed tests. This quality assurance and accreditation program is robust and rapidly growing, and has strong support in the laboratory testing community.

The CAP has monitored and commented on the Centers for Disease Control and Prevention (CDC) and CMS regulatory activities in the area of genetic testing, particularly in the review of the Notice of Intent to determine if changes to CLIA are needed specifically for genetic testing. In addition to the CDC and CMS activities, we have monitored the Food and Drug Administration (FDA) and its activities in the development of a pre-market review template for genetic tests and most recently FDA's consideration of re-opening the Analyte Specific Reagent (ASR) rule. While these regulatory initiatives are considered, the CAP is moving forward on proposed enhancements to our programs in efforts to address anticipated needs in genetic testing based on our long-established commitment to quality laboratory practices.

In summary, the College of American Pathologists understands the challenges that exist to assure high quality genetic testing, and it is absolutely committed to that end. We look forward to working with the CLIA, HHS and its agencies, and professional

organizations to achieve this goal. In particular, the College would specifically welcome the opportunity to return to this committee at a future date to provide a more comprehensive overview of the CAP's efforts. On behalf of the CAP, I thank you for this opportunity to speak to you today.