Association for Molecular Pathology Position Statement:
Oversight of Laboratory Developed Tests

Background:

AMP is an international medical and professional association representing approximately 1,800 physicians, doctoral scientists, and medical laboratory scientists who perform laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Our members are dedicated to the development and implementation of molecular pathology testing, including genetic testing, in a manner consistent with the highest standards established by the Clinical Laboratory Improvement Amendments (CLIA), the College of American Pathologists (CAP), the American College of Medical Genetics (ACMG), and the Food & Drug Administration (FDA). AMP members populate the majority of clinical molecular diagnostics laboratories in the United States, and their efforts are central to the generation of novel, high quality, molecular tests that are applied daily in medical decision-making. Assays designed and validated within these laboratories are used for diagnosis, prognosis and patient management in all medical areas including cancer, infectious diseases, heritable disorders, and histocompatibility testing. In addition to developing and implementing such tests, AMP members are experts in their interpretation.

In recent years, there has been increased attention on the oversight of laboratory developed tests (LDTs) among policy makers, manufacturers, regulators and the laboratory community. These discussions include proposed changes to the current oversight mechanisms for LDTs, such as the creation of registries, expansion of FDA enforcement, strengthening of the CLIA program, and others. While AMP believes that current mechanisms are sufficient in ensuring patient safety and broad access to high quality tests, AMP is taking this opportunity to elucidate our position on the issue.

AMP Believes:

- LDTs are an essential and central component of medical practice. Anatomic and clinical pathologists as well as other laboratory professionals who perform such tests have, and will continue to have, vital roles in therapeutic decision-making and other aspects of patient management.

- There is no evidence that the comprehensive system of oversight already in place has been inadequate, or that there are systemic problems with the quality of U.S. laboratory tests performed in compliance with CLIA or with LDTs specifically.

- Laboratory directors are pathologists, doctoral scientists, or other medical professionals in compliance with CLIA who have undergone extensive and specialized training in the design and development of LDTs as well as their analytic and clinical validation. Laboratory directors are experts in assay quality control and quality assurance methods and procedures.

- For the vast majority of molecular pathology tests, the CLIA program, laboratory accreditation by professional societies such as the CAP, and board certification and licensure of laboratory

directors provide the most effective, appropriate, and patient-oriented oversight system for clinical diagnostic laboratories.

• Laboratories performing molecular tests are subject to general CLIA requirements and CLIA personnel requirements for high-complexity testing.

• Only high quality, clinically and analytically valid diagnostic tests should be performed in clinical laboratories. All tests are required to be validated and performing laboratories should meet CLIA standards, adhering to established guidelines.

• CLIA requires that laboratories address analytical validity and, through the clinical consultation requirements, address clinical validity as well.

• CLIA establishes the following responsibilities for the laboratory director and AMP believes all LDT developers should ensure:

- The quality of all aspects of tests performance and results reporting
- That the physical and environmental conditions of the laboratory are appropriate and safe
- Enrollment in HHS-approved proficiency testing programs
- Employment of sufficient personnel with appropriate education, experience, training and competency required for patient testing
- Establishment of policies and procedures for personnel competency assessment and monitoring
- Specification of the responsibilities and duties of each consultant, supervisor and employee
- Compliance with applicable requirements and regulations
- Documentation of the clinical validity of the test
- Retention policies are consistent with the laboratory quality assessment activities

• In addition to ensuring necessary access to innovative tests, the current oversight system allows clinical laboratorians to rapidly incorporate new findings into practice, and to modify existing laboratory tests and their usage in accordance with advances in our understanding of clinical utility and disease pathogenesis. In the molecular pathology laboratories, LDTs have played key roles in the major advancements we have made in the diagnosis and management of diseases such as AIDS, leukemia, lymphoma, and other types of cancer. LDTs identify suitable bone marrow donors, and allow us to monitor the disease course in transplant recipients.

• With the vast majority of molecular pathology tests regulated by the CLIA program, mandating FDA oversight for all LDTs would hinder innovation and the practice of medicine as all specialties use diagnostic tests.

• When developing a new procedure or diagnostic approach, clinicians draw on their experience, expert medical judgment, and act within the regulatory framework. Similar to other specialties, pathologists and molecular pathologists in particular develop new applications to adapt to changes in practice. Nimbleness in developing new tests is crucial to respond to public health

challenges. This was evident during the 2009 H1N1 pandemic influenza outbreak where laboratories were developing and validating diagnostic tests to rapidly detect the virus and its spread.

AMP Recommends:

- Laboratory directors or medical directors should review and reaffirm their policies and procedures for reviewing and documenting that appropriate validation studies have been performed for all tests developed in their laboratories with due consideration of clinical utility and clinical utilization.

- CLIA should reassess utilization of resources and enforcement capabilities in order to meet its current mandate. CLIA should strengthen its enforcement capabilities by hiring more inspectors and improve the training of its inspectors.

- To increase transparency, CMS should make information collected from laboratories in the CLIA program available and easily accessible by the public and regulators.

- Proficiency testing should be required. When proficiency testing is not available, laboratories should perform alternative assessments as directed by CLIA.

- Some tests may require greater scrutiny, such as those with hidden or nontransparent algorithms, and should be subject to additional review by regulators.

- All LDTs should be subject to the same oversight mechanisms, and molecular tests should not be treated exceptionally.

- Any changes to the current oversight system should occur after a formal rule making process or statutory change.

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