



Statement of

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President Elect

of

The American Society for Clinical Pathology

before

**The U.S. Food and Drug Administration
Center for Devices and Radiological Health**

Public Meeting:

**Oversight of Laboratory Developed Tests
(LDTs)**

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I am John E. Tomaszewski, MD, FASCP, President Elect of the American Society for Clinical Pathology (ASCP), a professional medical society that provides excellence in education, certification, and advocacy on behalf of patients, pathologists and laboratory professionals. I am also Interim Chair of Pathology at the University of Pennsylvania in Philadelphia. I am here on behalf of ASCP's 130,000 member pathologists and laboratory professionals, many of whom develop and perform laboratory developed tests (LDTs).

I am pleased to announce that this statement is also endorsed by the Joint Commission. The Joint Commission has been evaluating and accrediting hospital laboratory services since 1979 and freestanding laboratories since 1995. Today, The Joint Commission accredits almost 2,000 organizations providing laboratory services. This represents almost 3,000 Clinical Laboratory Improvement Amendment-certified laboratories, including freestanding laboratories, such as reference labs and in vitro fertilization labs, and those connected with other health care organizations such as ambulatory surgical centers and long term care facilities.

ASCP appreciates this opportunity to appear before the U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health for this hearing of issues related to the regulation of laboratory developed tests. ASCP thanks the organizers of this meeting for recognizing the need to ensure the highest quality laboratory testing.

Laboratory developed tests or LDTs are increasingly being integrated into standard practice for diagnosing and managing disease, predicting the risk of developing disease, and informing decisions about lifestyle and behavior. These tests are enabling improved prevention, treatment, and disease management for an array of common chronic conditions such as cancer, heart disease, and diabetes, as well as rare genetic disorders. They have become indispensable tools in the practice of medicine. As a patient-centric organization, ASCP's mission is to protect patient safety while promoting advances in medicine. ASCP and its membership strongly believe that all diagnostic tests should be of the highest quality, reliability, and safety, and that each test should provide valid and useful information for clinical decision-making.

While LDTs represent the leading edge of clinical testing being offered to patients today, and have a solid record of advancing patient care safely and effectively, ASCP feels that the time has come for the FDA to insert its regulatory authority over high complexity LDTs. There must be assurances that these tests are clinically valid, performed correctly by competent laboratories, and the results communicated to patients by clinicians adequately trained to interpret them. ASCP supports strengthened oversight to ensure that LDTs remain one of the key tools clinicians can use to answer increasingly complex questions regarding patient care.

Evaluation of LDTs, as with any other diagnostic test, should include the test's analytic and clinical validity. Under the Clinical Laboratory Improvement Amendments (CLIA) of 1988,

laboratory directors and technical supervisors are responsible for ensuring that test methods are both appropriate for the intended clinical application and provide quality results. ASCP supports a risk-based approach to regulation through enhanced coordination between the FDA and the federal CLIA regulating agencies. While high complexity LDTs should fall under the purview of the FDA, LDTs of moderate complexity, those not deemed to be “in vitro diagnostic multivariate assays” should continue to be regulated by CLIA. ASCP recommends an enhanced accreditation process of oversight through a combination of governmental and non-governmental organizations. The CLIA regulatory process must ensure that data is collected that substantiates claims of clinical validity. Accrediting bodies may also have a role to play in this process.

ASCP also supports the recommendation of the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS) in their May 2008 report that CLIA require proficiency testing (PT) for all non-waived genetic laboratory tests for which PT products are available, and that the Department of Health and Human Services fund studies to evaluate alternative performance assessment methods. A balanced approach will be essential to evaluate the reproducibility of these assays with a protocol that maintains the advantages of multi-site PT, but also addresses the risks of inter-laboratory variation.

Clinical utility, however, remains a subjective standard dependent on how clinicians utilize assay results in managing patient treatment, and not on an objective quality inherent in the test method. ASCP is concerned that requiring proof of clinical utility as a pre-requisite for marketing of these assays might impede or even prevent patient access to them. The nature of these molecular assays allow for nimble clinical intervention utilizing the latest published research. These assays can be quickly modified to take advantage of the latest findings in a rapidly advancing area of medicine. A lengthy approval process that requires evidence of clinical utility might hinder the development of these assays, thus preventing researchers from implementing translational findings into clinical practice.

The past decade has provided many examples of the impact of these nimble assays on the treatment and prognosis of disease. AIDS, once a terminal illness is now a manageable chronic disease thanks to laboratory developed tests that are now used to diagnose and treat HIV. The treatment for chronic myelogenous leukemia or CML, which accounts for 20% of all adult leukemias, has changed drastically in recent years as LDTs afford afflicted patients targeted therapies that can achieve molecular remission as well as hematologic remission thereby offering a cure for this devastating disease. Likewise, the ability to respond rapidly has allowed LDTs to play a critical role in the identification of West Nile virus, avian flu, and acute respiratory syndrome (SARS), thus protecting the public’s health.

ASCP is also concerned that lengthy approval procedures would delay implementation of new tests, stifle innovation, increase development costs, and thus limit patient access to potentially

beneficial assays. Low volume LDTs, such as those for rare genetic tests, could experience difficulty attaining approval because of the small populations that would be available for clinical trial testing. Moreover, smaller laboratories, particularly laboratories at academic medical centers that have historically been major sites of innovation for LDTs, could be forced to abandon this area of testing, precluding patients from cutting-edge therapeutics.

At this early stage of the genetic diagnostic era, it is vital that FDA strike the right balance in asserting their authority over the regulation of laboratory developed tests. The regulatory infrastructure adopted must be sufficiently meticulous to safeguard the public without being so burdensome that it impedes the emerging technology.