



Session Title	CAP Role	CAP Speaker
Components of a Test and LDT Labeling Considerations	Public Comments (4 min)	George Kwass

Good morning. My name is George Kwass and I am Chief of Staff and Laboratory Director at Holy Family Hospital at Merrimack Valley in Haverhill, Massachusetts. I am speaking on behalf of the College of American Pathologists. The CAP represents 18,000 pathologists who practice clinical and/or anatomic pathology in community hospitals, independent laboratories, academic medical centers, and federal and state health facilities. With extensive experience as a quality standards-setting organization, the CAP accredits more than 7,000 laboratories and enrolls some 23,000 laboratories in its Proficiency Testing (PT) programs.

We appreciate this opportunity to participate in this public workshop and provide the FDA with the College's recommendations on the agency's proposal for a risk-based framework for addressing the regulatory oversight of laboratory developed tests (LDTs). Further, over the next two days, the College will provide its comments on the specific components of a laboratory test (LDT) and LDT labeling considerations, and outline our key concerns.

CAP believes a laboratory developed test must possess the following characteristics:

1. The test is performed by the clinical laboratory in which it was developed; and
2. The test has not previously been approved or cleared by FDA as an in vitro diagnostic device.



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A laboratory is considered to have developed a test if the test *procedure* was created by and implemented in that laboratory, irrespective of whether fundamental research underlying the test was developed elsewhere or reagents, equipment, or technology integral to the test was purchased, adopted, or licensed from any other entity.

An LDT may or may not employ ASR, RUO, or IUO reagents; the type(s) of reagent(s) and device(s) employed does not affect whether a test is classified as an LDT. CAP believes that use of RUO and IUO reagents, instruments, and systems as components of LDTs should be permissible in clinical diagnosis and patient management when the test has been validated by the laboratory personnel.

LDTs are not restricted to any particular test methodology. LDTs may rely on biochemical, genetic, morphological or other techniques. Examples of LDTs include genetic tests for breast cancer and tests for emergent and fatal infectious diseases such as herpes encephalitis and H1N1 influenza.

The FDA's definition of LDTs would exclude many innovative LDTs developed and used within healthcare systems. We have heard concerns from our members that as written the guidance would impact their ability to provide appropriate and critical testing for their patients.

Due to the additional layers of review that laboratories comply with through CLIA regulations, the CAP believes tests incorporating ASRs, RUOs or IOUs should not be excluded from the definition of an LDT. Tests that include these components are validated by professional laboratory personnel and should not be excluded based on the



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provenance of reagents. Test validity must be verified regardless of where the components originate.

We believe the FDA definition should be expanded to include healthcare systems. We define healthcare systems as entities incorporated as a healthcare network. Healthcare systems also encompass including anyone within network, such as qualified providers ordering tests.

We believe transparency is critical and the most important part of any regulatory framework should enable patients and clinicians to understand the benefits and limitations of LDTs. Therefore, we believe for each LDT that a standard statement should be included on the test and performance data are made available upon request.

- CAP LDT Labeling statement: “The [name of test] used to produce this report was developed and performance characteristics determined by Laboratory X.”
- Analytical and clinical validity data must be available.

Thank you.



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Day 1: Thursday, January 8, 2015

Session Title	CAP Role	CAP Speaker
Clinical Validity/Intended Use	Public Comments (4 min)	Emily Volk

Good afternoon. My name is Emily Volk and I am the Regional Medical Director of the Department of Laboratory Medicine and Pathology at the Baptist Health System in San Antonio, Texas. I am speaking on behalf of the College of American Pathologists. As noted by Dr. Kwass earlier today, the CAP represents 18,000 pathologists who practice clinical and/or anatomic pathology in community hospitals, independent laboratories, academic medical centers, and federal and state health facilities. CAP has extensive experience as a quality standards-setting organization. We accredit more than 7,000 laboratories and enroll as many as 23,000 laboratories in its Proficiency Testing (PT) programs.

Pathologists serve as Lab Directors and, as part of our professionals' duties we are responsible for assuring that all the tests are clinically valid. We have extensive experience validating tests. We define clinical validity as a test's ability to detect or predict a disorder, identify a prognostic risk or other condition, or to assist in physicians in the management of their patients.

In defining the clinical validity of a test, we also review reference limits, reference intervals, clinical sensitivity, and specificity and clinical decision limits.

The qualities I have cited represent the primary performance measurements that are used to describe the clinical capabilities of a test. Other measures of clinical validity may be applicable in specific circumstances. This includes as genetic testing in which penetrance may become an element of clinical validity that may be examined.



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In the draft guidance the FDA proposes that a change in specimen type constitutes a new LDT. The CAP recognizes that laboratories may modify an existing LDT to improve performance. For example, some laboratories have modified a test to automate a manual method. The clinical claim and performance characteristics for the test do not change. In this case, the CAP believes the change should not constitute the creation of a new LDT. However, we acknowledge that a major analytic change or new clinical claim to an existing LDT creates the need for a new LDT designation.

Thank you.



**Session3: Categories for Continued Enforcement Discretion
List of Panelists**

Panel Discussion moderated
by Derek Scholes (NIH)

Emily Volk (College of American Pathologists)
Curtis Hanson (Mayo Clinic)
Roger Klein (Association for Molecular Pathology)
Laura Koontz (Ovarian Cancer National Alliance)
TBD (American Association for Cancer Research)



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Day 2: Friday, January 9, 2015

Session Title	CAP Role	CAP Speaker
Process for Classification and Prioritization	Public Comments (4 min)	Gail Vance

Good afternoon. My name is Gail Vance and I am the Director of the Division of Diagnostic Genomics at the Indiana University in Indianapolis, Indiana. I am speaking on behalf of the College of American Pathologists. As noted was noted yesterday, the CAP represents 18,000 pathologists who practice clinical and/or anatomic pathology in community hospitals, independent laboratories, academic medical centers and federal and state health facilities. CAP has extensive experience as a quality standards-setting organization, the CAP accredits more than 7,000 laboratories and enrolls as many as 23,000 laboratories in its Proficiency Testing (PT) programs.

I'd like to make three brief points regarding the proposed guidance, the role of pathologists, and an optimal risk classification scheme.

We believe that the process for classification and prioritization should be based on risk and the novelty of the LDTs. Our proposed approach views high-risk LDTs as proprietary algorithm tests that should require FDA review. Based on the draft guidance as written, we estimate 1,000 LDTs considered to be companion diagnostics will be classified as high-risk LDTs and require PMAs despite these tests being well-established in medical practice and the standard of care.

We believe that pathologists' participation is critical throughout the LDT process, because we already work in concert with other clinicians to improve the development application, interpretation, and dissemination of laboratory tests.



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Further, we believe that the pathologists should be involved in the prioritization process because we have expertise in the clinical and anatomic pathology laboratory specialties such as microbiology, immunology, chemistry, hematology, immunohematology, cytopathology, histopathology, genetic testing and informatics. In addition, pathologists have a long history of being responsible for the overall operation and administration of the laboratory, including the employment of personnel who are competent to perform test procedures; record and report test results promptly, accurately and proficiently; and assure compliance with the applicable regulations. We also ensure that testing systems developed and used for each of the tests performed in the laboratory provide quality laboratory services for all aspects of test performance, including the pre-analytic, analytic, and post-analytic phases of testing.

Finally, we believe that it is important to weigh the following factors in risk-classifications of LDTs. They are:

- Integration in medical practice (ie, existence of practice guidelines)
- Availability of proficiency testing
- Type of tests (screening, prognostic, diagnostics)

Thank you.



Session 6: Quality Systems Regulations
List of Panelists

Panel Discussion moderated by
Larry Brody (NIH)

Gail Vance (College of American Pathologists)
Andrew Hoofnagle (University of Washington)
Elaine Lyon (ARUP Laboratories)
Scott Patterson (Amgen)
Judith Wilber (CareDx)
Mickey Williams (NIH)