



Advancing Excellence

College of American Pathologists

**Comments to the
Food and Drug Administration on
Oversight of Laboratory Developed Tests
(Docket No. FDA-2010-N-0274)**

August 15, 2010

College of American Pathologists

1350 I Street, NW, Suite 590

Washington, DC 20005

(202) 354-7100

(202) 354-7155 – fax

(800) 392-9994

www.cap.org

INTRODUCTION

The College of American Pathologists (CAP) appreciates the opportunity to respond to FDA's request for comments regarding the oversight of laboratory developed tests, 75 Fed. Reg. 34463 (June 17, 2010). As discussed below, CAP has significant expertise in the assessment of laboratory quality, including assessment of the accuracy and reliability of laboratory developed tests (LDTs). Based on this experience, CAP believes that the FDA should implement a risk-based framework that leverages the resources of other expert bodies and enables FDA to focus on clinical claims made for high-risk LDTs. CAP shares FDA's goal of ensuring continued patient access to accurate, reliable, and innovative laboratory testing, and believes that FDA can best achieve this goal by implementing a new framework through a rulemaking process that is incremental, deliberative, and inclusive.

BACKGROUND

CAP is a national medical specialty society representing 17,000 board-certified pathologists who practice pathology and laboratory medicine. The College's Commission on Laboratory Accreditation (LAP) is responsible for accrediting more than 6,000 clinical laboratories worldwide. Our members have extensive expertise in providing and directing laboratory services and also serve as inspectors in the Centers for Medicare and Medicaid Services (CMS) deemed CAP accreditation program.

CAP also provides laboratories with a wide variety of proficiency testing programs and has the responsibility to evaluate the accuracy of test performance and interpretation in more than 20,000 laboratories worldwide. These programs are designed to improve the quality of laboratory services and to ensure the accuracy and reliability of diagnostic testing. The CAP accredits most of the sophisticated, high-complexity testing laboratories in the United States that develop and offer LDTs and has been assessing the performance of clinical laboratories for more than 50 years.

CAP is the leader in developing quality improvement programs for laboratories. CAP has been granted deemed status by the CMS, 42 C.F.R. § 493.553, through its Laboratory Accreditation Program (LAP). CAP accredits clinical laboratories based on standards that exceed CMS's regulations implementing the Clinical Laboratory Improvement Amendments of 1988 (CLIA), Pub. L. No. 100-578; 21 C.F.R Part 493, to ensure laboratory tests performed are accurate and reliable. Moreover, the CAP LAP standards are translated into detailed and focused Checklist questions, which provide a blueprint of quality practices for laboratories to follow, constantly evolve to reflect changes in technology and are tailored specifically to the test menu of individual laboratories.

CAP is delighted that FDA is considering the development of pilot programs for third party review of lower risk tests. See Webcast: FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests (July 19, 2010), available at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm> (presentation of Elizabeth Mansfield, Ph.D., Director for Personalized Medicine, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health). Just as CAP has been an integral part of ensuring laboratory compliance with CLIA through its deemed-status relationship with CMS, CAP hopes to work closely with FDA to ensure continued patient access to high quality LDTs and thereby to foster a shared mission of public health promotion and protection.

We believe that the CAP has unique insights into the benefits and risks presented by LDTs and the many practical issues surrounding their regulation. As medical specialists in the diagnosis of

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

disease, pathologists have a long track record of delivering high quality services to patients. Pathologists therefore have a keen interest in ensuring that the ability to provide high quality diagnostic services to patients and other physicians is not unduly restricted. Furthermore, as a CMS-deemed third-party accreditor of clinical laboratories, the CAP has had oversight responsibilities in a variety of laboratory settings, from complex university medical centers to physician office laboratories covering a complete array of disciplines and testing procedures available in today's laboratory.

CAP's PROPOSED FRAMEWORK FOR LDT OVERSIGHT

CAP believes oversight of LDTs should be strengthened based on a stratified schema that classifies tests based on their potential risks to patients. Moreover, analytic and clinical validation of LDTs should be required.

Over the past two years, CAP developed its proposed framework through a considered, deliberative process with stakeholder engagement in an effort to build consensus on an oversight proposal.

- **Definition of a Laboratory Developed Test**

LDTs have a long history of use by physicians to advance patient care. LDTs represent some of the most innovative clinical testing being offered to patients today. LDTs are fundamentally different from the types of medical devices traditionally regulated by FDA. LDTs are most often developed by a single testing laboratory for the purpose of providing information to physicians that informs patient care. Unlike medical devices regulated by FDA, LDTs are not developed as products for the purpose of commercial distribution outside of the developing laboratory. Moreover, the developing laboratory is subject to regulation under CLIA.

LDTs are developed and validated by the laboratory that performs clinical testing – LDTs are not “test systems” produced by independent manufacturers and sold as stand-alone products to testing facilities. Although there are currently several thousand LDTs used in clinical care, the vast majority of clinical laboratory tests performed today are not LDTs and rely on packaged test systems produced by independent manufacturers and sold to testing facilities. The large majority of LDTs are used ‘locally’ within a region and not marketed nationwide.

CAP believes that an LDT is a test developed within a CLIA-certified laboratory which is used in patient management and has both of the following characteristics:

- The test is performed by the clinical laboratory in which the test was developed; and
- The test is currently neither FDA-cleared nor FDA-approved.

- **Key Features of Oversight Framework**

CAP believes that the following features should be included in any oversight framework for LDTs:

- Tiered, risk-based regulation;
- Assurance of both analytic and clinical validity;

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

- Evaluation of risk based on the laboratory's claims. Risk defined as the potential for harm to patients of an incorrect or misinterpreted result when the test is ordered consistent with the laboratory's claims;
- Continued oversight of clinical laboratory quality by CMS and deemed accreditors under CLIA;
- FDA use of third party accreditors to validate low and moderate risk tests;
- Monitoring of laboratories offering low risk LDTs by CMS-deemed accreditors to ensure laboratory maintains adequate analytical and clinical validation;
- Prior review and approval of moderate risk LDTs by CMS-deemed accreditors to ensure that the laboratory has adequately validated the test analytically and clinically before testing is used in patient care;
- Targeted FDA review and approval of clinical claims for only high-risk LDTs, with oversight of compliance by laboratories performing high risk LDTs by CMS and CMS-deemed accreditors;
- Coordination between FDA and CMS to avoid duplicative or unduly burdensome requirements on laboratories;
- Regulatory flexibility to encourage innovation of new diagnostic and predictive tests to promote and protect public health;
- Continued ability of laboratory personnel to engage in patient-specific communications with physicians regarding test selection and interpretation.

- **Risk Classification Principles**

CAP believes that a tiered system, based on test risk, that leverages the expertise of CMS and third party accreditors, can best assure that tests being offered are analytically and clinically valid.

CAP recommends that LDT oversight be based on the following risk classification principles:

- Low Risk
 - The consequence of an incorrect result or incorrect interpretation is unlikely to lead to serious morbidity/mortality.
 - The test result is typically used in conjunction with other clinical findings to establish or confirm diagnosis.
 - No claim that the test result alone determines prognosis or direction of therapy.
- Moderate Risk
 - The consequence of an incorrect result or incorrect interpretation may lead to serious morbidity/mortality AND the test methodology is well understood and independently verifiable.
 - The test result may be used for predicting disease progression or identifying whether a patient is eligible for a specific therapy.
 - The laboratory may make claims about clinical accuracy.

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

- High Risk
 - The consequence of an incorrect result or incorrect interpretation could lead to serious morbidity/mortality AND the test methodology is neither well understood nor independently verifiable.
 - The test is used to predict risk of, progression of, or patient eligibility for a specific therapy to treat a disease associated with significant morbidity or mortality, AND;
 - The test methodology uses proprietary algorithms or computations such that the test result cannot be tied to the methods used or inter-laboratory comparisons cannot be performed.
- **Roles for Third Party Accreditation:**

The College recognizes the evolution of LDTs with respect to technology and complexity but maintains that the vast majority of these tests can utilize the CAP approach to assure quality laboratory testing allowing the FDA to focus its role more narrowly on high-risk LDTs. CAP believes third party accreditation organizations have an important role in the oversight of LDTs. The LAP program provides a well-established and nationally-recognized foundation for quality practices that promotes standards of excellence for laboratory testing, thus positively impacting patient care.

The LAP meets the needs of a variety of laboratory settings, from complex university medical centers to physician office laboratories. Moreover, LAP is the only program covering a complete array of disciplines and testing procedures available in today's laboratory. The program also accommodates all testing sites, ensuring consistent levels of service throughout institutions and health care systems.

CAP incorporates a continuous system of compliance assessment and process improvement into each step of the two-year accreditation cycle. Onsite inspection is used to verify compliance, to assess the overall quality of the laboratory, and to identify deficiencies that can affect the quality of laboratory performance. CAP staff works with laboratories to ensure that deficiencies are corrected and documented before accreditation can be granted. Throughout the following two years, CAP assists laboratories in maintaining continuous compliance. Approximately one year following the on-site inspection, the laboratory performs a self-assessment to ensure ongoing compliance with CAP standards and optimal laboratory performance.

FDA Must Engage in Notice-and-Comment Rulemaking In Order to Implement a New Framework for LDTs

As a matter of both law and public policy, CAP believes that FDA should implement a new regulatory framework for LDTs through notice-and-comment rulemaking. CAP is concerned that the Agency apparently intends to implement substantive new requirements for LDTs through guidance documents. At the July 19 public meeting, CDRH Director Jeffrey Shuren stated that notice-and-comment rulemaking is not required because the Agency does not intend to impose a "new requirement" on LDTs but merely intends to discontinue its longstanding policy of "enforcement discretion" and to enforce requirements that are already in place.¹

¹ Specifically, Dr. Shuren stated in response to a question from an audience member that the Agency had not included notice-and-comment rulemaking as an option for its path forward in regulating LDTs "because the requirements actually already apply now. The law is in effect." See Webcast: FDA/CDRH Public Meeting: Oversight of Laboratory Developed Tests (July 19, 2010), available at <http://www.fda.gov/MedicalDevices/NewsEvents/WorkshopsConferences/ucm212830.htm>. According to Dr. Shuren,

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

Based on CAP's understanding of the Administrative Procedure Act, we believe that FDA regulation of LDTs would constitute a substantive regulatory change requiring notice-and-comment rulemaking. 5 U.S.C. § 553. (See Appendix for additional analysis)

Conclusion

CAP believes that the current CLIA framework has resulted in LDTs that are highly accurate and reliable. CAP supports targeted oversight by FDA of high-risk LDTs, but believes that wholesale oversight by FDA of all LDTs is not feasible and could adversely affect public health by reducing patient access to laboratory testing. CAP proposes an oversight framework that leverages resources and expertise of other agencies and third parties. CAP believes that to minimize disruptions and ensure continued patient access to high quality tests, any new framework must be implemented through notice and comment rulemaking.

CAP appreciates the opportunity to participate in the July 19-20 meeting and to submit these comments. CAP looks forward to continue discussion with FDA regarding the development of an oversight approach for LDTs that advances our shared goal to encourage innovation and continue improvement of LDTs.

FDA had "as a matter of policy determined not to exercise or not to enforce that authority as of right now," but when the Agency decides to alter its enforcement discretion, either to "put it in place or take it back," FDA uses its "guidance process as a matter of policy" because "it's not imposing a new requirement, the requirements are already there." Id.

Appendix: Notice-and-Comment Rulemaking Analysis

Regulation of LDTs Would Constitute a Substantive Rule

CAP has been advised that, under the Administrative Procedure Act, an administrative agency must engage in notice-and-comment rulemaking in order to substantively alter a regulatory regime. See United States Telecom Ass'n v. FCC, 400 F.3d 29, 35 (D.C. Cir. 2005) (“[F]idelity to the rulemaking requirements of the APA bars courts from permitting agencies to avoid those requirements by calling a substantive regulatory change an interpretive rule.”); Appalachian Power Co. v. EPA, 208 F.3d 1015, 1024 (D.C. Cir. 2000) (a guidance document establishing a new regulatory regime constitutes a legislative rule for which notice-and-comment rulemaking is required); Alaska Prof. Hunters Ass'n, Inc. v. FAA, 177 F.3d 1030, 1034-35 (D.C. Cir. 1999) (holding FAA could not impose new requirements on hunters after more than thirty years of non-enforcement without providing opportunity to comment through rulemaking).

The D.C. Circuit's holding in Syncor Int'l Corp. v. Shalala, 127 F.3d 90, 95 (D.C. Cir. 1997), is particularly apposite here. In that case, the court held unlawful FDA's use of guidance to regulate as drugs positron emission tomography (PET) radiopharmaceuticals after more than a decade of enforcement discretion by the Agency. Similar to its history with LDTs, FDA had “made a careful, considered decision not to exercise the full extent of its regulatory authority” but subsequently changed course based on changes in both technology and medical practice. According to the Court, “[t]he reasons FDA has advanced for its rule—advancement in PET technology, the expansion of procedures in which PET is used, and the unique nature of PET radiopharmaceuticals—are exactly the sorts of changes in fact and circumstance which notice and comment rulemaking is meant to inform.” Id.

Although Dr. Shuren asserts that the comprehensive regulation of LDTs would not “impos[e] a new requirement” on the industry, it has been FDA's policy “since the implementation of the Medical Device Amendments of 1976” to exercise “enforcement discretion” and not “actively regulate []” most LDTs. See 75 Fed. Reg. 34,463, 34,463 (June 17, 2010). Thus, as LDTs have developed over the past generation, they have generally not been subject to the statutory and regulatory requirements for medical devices. Now, however, FDA is reversing course and proposing to regulate all LDTs as medical devices. Many LDTs that previously were subject to no FDA requirements would be subject to premarket approval or clearance, Quality System Regulation, labeling, and adverse event reporting, among other requirements. FDA's rationale for this sweeping change is that “LDTs are becoming more complex, [and] diagnostic tests are playing an increasingly important role in clinical decisionmaking and disease management, particularly in the context of personalized medicine.” Id. Contrary to the assertions of Dr. Shuren, these are “exactly the sorts of changes in fact and circumstance which notice and comment rulemaking is meant to inform.” Syncor Int'l Corp., 127 F.3d at 95.

Guidance Will Not Enable FDA to Achieve Its Objectives Because it Cannot Establish Legally Binding Requirements

CAP further understands that guidance documents cannot, as a matter of law, “create or confer any rights for or on any person.” FDCA § 701(h)(1)(A), 21 U.S.C. § 371(h)(1)(A). Further, it is our understanding that, according to FDA's own regulations, guidance documents “do not establish legally enforceable rights or responsibilities” or “legally bind the public or FDA.” 21 C.F.R. § 10.115(d)(1). FDA historically considered guidances to constitute the “the formal

position of FDA," a position that was overturned by Community Nutrition Institute v. Young, 818 F.2d 943 (D.C. Cir. 1987); 44 Fed. Reg. 22,323, 22,335 (Apr. 13, 1979), "into question FDA's procedure for issuing advisory opinions and guidelines that purport[ed] to bind the agency and thereby constrain the agency's discretion."; 62 Fed. Reg. 8961, 8963 (Feb. 27, 1997). Subsequently, Congress amended the Federal Food, Drug, and Cosmetic Act (FDCA) to clarify that FDA must promulgate rules—not issue guidance documents—in order to create legally enforceable requirements. See FDA Modernization Act of 1997 (FDAMA), Pub. L. No. 150-115, § 405, 111 Stat. 2296, 2368 (1997); 21 U.S.C. § 371(h)(1)(A); 21 C.F.R. § 10.115(d)(1); see also Gen. Elec. Co. v. EPA, 290 F.3d 377, 382-83 (D.C. Cir. 2002) (document identified as a "guidance" is a legislative rule because it purports to bind regulated entities and the agency).

FDA's stated basis for reconsidering its policy of enforcement discretion is to better protect public health. 75 Fed. Reg. at 34464. Presumably, improved public health protection will involve increased FDA enforcement. However, a precondition for enforcement is that there be enforceable regulatory requirements. Guidance documents are by their nature not enforceable. Therefore, if FDA wishes to develop binding legal requirements for LDTs the Agency needs to proceed through notice-and-comment rulemaking.

Implementing New Requirements for LDTs through Rulemaking Constitutes Good Policy

- **Rulemaking Will Allow FDA to Create a Flexible, Risk-Based Framework that Accounts for the Unique Nature of LDTs**

FDA has indicated that it wishes to create a "risk-based" oversight framework for LDTs. 75 Fed. Reg. at 34,464. For those LDTs that fit within existing device classification regulations, the issuance of guidance may be sufficient. Under the device provisions of the FDCA, however, all unclassified LDTs that are not substantially equivalent to currently marketed Class I or Class II devices would be automatically classified as Class III devices, subject to the most stringent FDA oversight, including premarket approval. See 21 U.S.C. § 360c(f). In order to avoid this result, FDA would either have to respond to individual petitions requesting reclassification, which could quickly overwhelm the Agency, or engage in notice-and-comment rulemaking to establish regulations classifying certain categories of LDTs as Class I or Class II devices exempt from premarket approval or clearance. As a practical matter, then, it is likely that the Agency will be required to engage in notice-and-comment rulemaking at some point in order to implement the risk-based framework that FDA hopes to achieve, and a prospective rulemaking process would be most efficient.

- **Rulemaking Will Allow The Opportunity For Communication and Knowledge-Sharing Between FDA and Laboratories**

Given our extensive experience as a CMS-deemed accreditor, CAP believes that laboratories will have difficulty adapting to FDA's regulatory approach due to the significant "language barrier" between laboratories, who are largely unfamiliar with the Agency's requirements or culture and the FDA, which has limited experience regulating clinical laboratory activities. A significant amount of education of both laboratories and the Agency will be required in order for any new regulatory framework to be implemented successfully.

Compounding the "language barrier" is the fact that there currently is no binding, enforceable definition of "laboratory-developed test" in either the FDCA or FDA's regulations. In one Federal Register notice, FDA described LDTs as "tests that are developed in-house by clinical laboratories." See, e.g., 62 Fed. Reg. 62243, 62249 (Nov. 21, 1997).

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

Similarly, in a draft guidance, FDA has asserted that “LDTs are tests that are developed by a single clinical laboratory for use only in that laboratory.” FDA, Draft Guidance for Industry, Clinical Laboratories, and FDA Staff: In Vitro Diagnostic Multivariate Index Assays (July 26, 2007).

If FDA intends to create a comprehensive oversight regime for LDTs, at a minimum, FDA regulations should provide a standard, enforceable definition of the term so that industry and the Agency know what products are subject to regulation. See Appalachian Power Co., 208 F.3d at 1024; see also Office of Management and Budget, Final Bulletin for Agency Good Guidance Practices, 72 Fed. Reg. 3432, 3438 (Jan. 25, 2007) (encouraging agencies to consider utilizing notice-and-comment rulemaking for “interpretive significant guidance documents that effectively would extend the scope of the jurisdiction the agency will exercise [or] alter the obligations or liabilities of private parties”). Creating a binding, enforceable definition requires rulemaking.

o **Rulemaking Will Best Enable An Orderly Transition To a New Regulatory Regime**

Notice-and-comment rulemaking ensures that FDA develops a considered regulatory approach that incorporates the views and addresses the concerns of regulated entities and thereby minimizes the opportunity for negative unintended consequences. FDA’s approach to regulating analyte specific agents (ASRs) stands in marked contrast to its recently-abandoned attempt to regulate in vitro diagnostic multivariate assays (IVDMIA)s² and therefore provides an illustrative case study regarding the value of rulemaking. By engaging in notice and comment rulemaking for ASRs, see 61 Fed. Reg. 10,484, 10,484 (Mar. 14, 1996), FDA was able to receive and incorporate comments from all interested stakeholders and was able to create valid, enforceable rules for both industry and the Agency with respect to ASR classification, see 21 C.F.R. § 864.4020, labeling, id. § 809.10(e) and distribution, id. § 809.30. In sharp contrast, FDA’s use of guidance to address a subset of LDTs, known as In Vitro Diagnostic Multivariate Index Assays (IVDMIA)s, without engaging in notice-and-comment rulemaking, led to significant confusion for affected stakeholders, disrupted business plans³ and the LDT marketplace, and ultimately failed to produce a coherent regulatory framework.⁴

² After nearly four years and the receipt of 172 comments, FDA has signaled that it intends to abandon its IVDMIA guidance in favor of a broader approach to LDT oversight. See Turna Ray, FDA Shelves IVDMIA Final Guidelines in Order to Focus on Overall LDT Regulation, PHARMACOGENETICS REP., June 17, 2010.

³ See, e.g., Transcript, FDA Public Meeting on IVDMIA)s 114-20 (Feb. 8, 2007) (testimony of InterGenetics CEO Craig Shimasaki on the detrimental impact of FDA’s decision, one month before the company’s predictive breast cancer test was set to launch, to reverse its prior position that FDA approval or clearance was not required as long as the test was performed at a CLIA-accredited laboratory and was not sold as a test kit and to instead require the submission of a premarket approval application).

⁴ Many of the comments submitted to FDA expressed concern about FDA’s use of guidance documents to effect such a significant regulatory change. See, e.g., Advanced Medical Technology Association, Comments to the Docket, FDA-2006-D-0233, at 2 (Mar. 5, 2007) (asking how FDA “intend[s] to establish new regulatory requirements with a guidance document that by definition is not binding in nature”); Association for Molecular Pathology, Comments to the Docket, FDA-2006-D-0233, at 2 (Mar. 2, 2007) (“AMP respectfully requests that . . . FDA convene a classification panel (e.g., as was done in the reclassification of immunohistochemistry tests) so that criteria for determining which tests will be subject to FDA regulation will be transparent to laboratories developing such tests.”); American Clinical Laboratory Association, Comments to the Docket, FDA-2006-D-0233, at 1 (Feb. 8, 2007) (“ACLA recommends that FDA issue a proposed rule to address this important subject matter through the formal notice and comment rulemaking process rather than through sub-regulatory guidance.”); see also American Society for Clinical Laboratory Science, Comments to the Docket, FDA-2006-D-0233, at 3 (Mar. 5, 2007) (expressing concern that, with the issuance of the draft guidance on IVDMIA)s “there does not seem to be the same level of communication between the agency and stakeholders that we see in a rulemaking process”). These concerns are magnified here, as FDA seeks to regulate a much broader range of tests.

IVDMIAAs are merely a small region of the vast universe of LDTs that FDA now seeks to regulate. Because of the myriad issues raised with regulating a new product class and the unique nature of the products at issue, if the Agency attempted to proceed by issuing guidance rather than by using notice-and-comment rulemaking, it would be similarly likely to lead to a host of unintended consequences. FDA itself has recognized that LDTs have become increasingly important in clinical decisionmaking and disease management, see 75 Fed. Reg. at 34,463, and the issuance of guidance purporting to regulate all LDTs as medical devices would likely cause a disruption in the LDT marketplace, which could ultimately present a risk to the public health by denying healthcare providers and their patients access to important tests.

FDA has minimized the disruptive effect of major regulatory change in the past by engaging in notice-and-comment rulemaking with full participation from all interested stakeholders. For example, FDA used an incremental notice-and-comment rulemaking approach when instituting a regulatory scheme for human cellular and tissue-based products (HCT/Ps). See 58 Fed. Reg. 53248 (Oct. 14, 1993) (statement of policy indicating that FDA has jurisdiction over human cells intended for use as somatic cell therapy and would regulate them pursuant to its authority over biological products and drugs); 58 Fed. Reg. 65514 (Dec. 14, 1993) (interim rule creating the Part 1270 regulations); FDA, Proposed Approach to Regulation of Cellular and Tissue-Based Products 6 (Feb. 1997); 62 Fed. Reg. 9721 (Mar. 4, 1997) (public workshop regarding announcement of proposed approach to the regulation of HCT/Ps); 63 Fed. Reg. 26744 (May 14, 1998) (proposed Part 1271 regulations); 66 Fed. Reg. 1508 (Jan. 8, 2001) (soliciting public comments regarding the regulation of HCT/Ps); 69 Fed. Reg. 29786 (May 25, 2004) (final Part 1271 regulations). FDA could have argued that rulemaking was unnecessary on the basis that HCT/Ps are biological products subject to the Agency's jurisdiction, but FDA did not do so. As a result of its decision to act deliberately and incrementally and to engage meaningfully with those potentially affected by the changes, there was an orderly transition to a new HCT/P regulatory regime for FDA, the regulated industry, and the public. FDA should take a page from its HCT/P playbook and act through stepwise, incremental notice-and-comment rulemaking when developing its approach toward regulating LDTs.

- **Rulemaking Will Best Prevent The Imposition of Duplicative or Conflicting Requirements On Laboratories**

CAP is concerned that FDA oversight will lead to a situation in which laboratories are subject to duplicative or conflicting regulations by CMS and FDA. Both CLIA and FDA medical device regulations contain inspection, validation, and reporting requirements. For example, laboratories are already obligated under CLIA to establish the analytic performance characteristics of every test offered; [42 U.S.C. 263 a(d)(1)]. The clinical consultant is required by law for assuring that test results include pertinent information required for specific patient interpretation and for assuring that clients are assisted in test ordering to meet clinical expectations. Thus, FDA requirements for analytic validation could impose needless additional burdens on laboratories without providing additional assurance of test accuracy.

Post-market surveillance is another area covered by both CLIA and FDA medical device regulations. Under CLIA, laboratories are subject to continuous monitoring by CMS and accreditation organizations, through the requirement to perform proficiency testing and conduct quality assessment.

CAP is particularly concerned about the negative impact that FDA labeling requirements could have on the ability of laboratories to communicate with health care providers. CLIA

CAP Comments to FDA Re: Oversight of Laboratory Developed Tests

requires the laboratory director to be assist clinicians in test selection and interpretation. However, FDA labeling requirements could be construed to prevent necessary communications between laboratory personnel and health care providers, to the detriment of patient care.

In developing a framework for LDTs, FDA should appreciate the CLIA regulatory framework with which laboratories already must comply and ensure that any new requirements for LDTs do not impose duplicative or inconsistent regulations. The rulemaking process best enables stakeholders to review proposed regulations and provide FDA feedback regarding the impact of such proposals on existing laboratory obligations.